ELECTROCARDIOGRAPHY

AND

CLINICAL DISORDERS

OF THE

HEART BEAT

BOOKS BY SIR THOMAS LEWIS

THE MECHANISM AND GRAPHIC REGISTRATION OF THE HEART BEAT

LECTURES ON THE HEART

THE SOLDIER'S HEART AND THE EFFORT SYNDROME

BLOOD VESSELS OF THE HUMAN SKIN AND THEIR RESPONSES

DISEASES OF THE HEART DESCRIBED FOR *PRACTITIONERS AND STUDENTS*

CLINICAL SCIENCE ILLUSTRATED BY PERSONAL EXPERIENCES

VASCULAR DISORDERS OF THE LIMBS DESCRIBED FOR PRACTITIONERS AND STUDENTS

RESEARCH IN MEDICINE AND OTHER ADDRESSES

PAIN

EXERCISES IN HUMAN PHYSIOLOGY (PREPARATORY TO CLINICAL WORK)

DISEASES OF THE HEART

Printed in Great Britain

ELECTROCARDIOGRAPHY

AND

CLINICAL DISORDERS

OF THE

HEART BEAT

A HANDBOOK FOR PRACTITIONERS AND STUDENTS

by the Late SIR THOMAS LEWIS

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PUBLISHER'S NOTE

Sir Thomas completed this work just before his death. In it he has revised and combined two of his earlier works, Clinical Disorders of the Heart Beat and Clinical Electrocardiography. These two books have passed through six and seven editions respectively, and the author felt that the time had come for integrating their subject matter into one volume.

As in his earlier works Sir Thomas prepared the manuscript of this book with great care and precision. Few authors have paid so much attention to the use of words and the construction of sentences.

It was the clearness of the manuscript and the generous assistance of some of his old pupils and colleagues that enabled this last, and perhaps greatest, of Sir Thomas Lewis' works to be placed at the disposal of the medical profession.

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PREFACE

Thirty five years ago I was led to search for a series of relatively simple tests based upon enquiry into the clinical histories of patients and upon bedside methods by which the common disorders of the heart beat might be recognised. For this purpose I made a large number of observations and incorporated in a handbook the new information so gathered with that gained from the contemporary writings of my co-workers. There are few important disorders of the heart beat which the practised senses may not recognise unaided. A single and portable piece of apparatus may be used in cases of doubt to supplement the observations so obtained. The Dudgeon sphygmograph is probably familiar to most medical men; it will readily trace a short curve from the radial pulse. Such a curve, especially if it be accompanied by a record of time, will usually complete an analysis of any common disorder of the heart beat.

The purpose of the handbook then was simply to recount such symptoms and signs as I found useful in identifying these disorders without recourse to complex graphic methods.

Simultaneously I was studying these and other disorders with the aid of the string galvanometer, a method then in its infancy and unknown in this country. These studies were published in the form of a second handbook.

While *Clinical Disorders of the Heart Beat* attempted to collect the simple bedside signs of disordered heart action and to narrate their influence upon prognosis and treatment in a manner palatable to practising clinicians, *Clinical Electrocardiography* was intended to supplement that book and to serve as an introduction to students of electrocardiography and as a guide to practitioners and hospital physicians in understanding curves taken by others from patients in their charge. It described in outline the most precise method that we possess when we attempt to identify the many forms of disordered heart action. It not infrequently happens that other graphic methods fail to analyse these disturbances

electrocardiography is the last court of appeal and its judgment is almost infallible. There are types of heart action upon which other methods are nearly if not quite silent. Knowledge of these conditions is in the almost *exclusive possession of electrocardiography*. *Finally*, the electrical curves provide a number of signs, associated with *abnormal* distribution of the muscular masses in the heart with abnormalities in the course taken by the excitation wave in the heart, or with recent injury of the muscle.

The two books have passed through six or seven editions and the demand for them appears to continue. But the reason *for* separating the subject matter of the two is no longer so clear as it was. Electrocardiographic records have become much more accessible and the need for their use in practice has greatly increased. Moreover, my small handbook of electrocardiography, standing by itself, has always suffered from the defect that it included little or nothing of the clinical applications, which were already covered by the first handbook which it supplemented. It seems that a more generally useful purpose will now be served if the material of these two books is brought thoroughly up to date and under one cover. The electrocardiographic sections have been enlarged, *mainly by freer illustration*. *They are still maintained in* relatively simple form, since they are intended for general use, and the theory of electrocardiography and the evidence relating to disordered heart action, which more advanced students may require, is set forth in my large treatise, The Mechanism and graphic Registration of the Heart Beat, and in contemporary works covering the same subjects.

The lack of uniformity in the time markings of the curves is due to their selection over a period of many years *during which method of recording has changed*. I *could* not keep the records uniform without sacrificing valuable illustrations. The time marker intervals are clearly inscribed in each separate figure, with the exception of simple pulse curves, which consistently include fifths of seconds at the top of each strip.

THOMAS LEWIS

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CHAPTER I

THE ELECTROCARDIOGRAPHIC METHOD

That electrical currents are developed in the heart at each contraction of this organ was demonstrated in the middle of the nineteenth century. Modern electrocardiography has originated from this discovery. The currents are small, yet modern instruments are sufficiently sensitive to record them with facility. It is unnecessary that the heart should be exposed; the currents will deflect a suitable galvanometer when the latter is connected to the limbs of the human subject, as Waller first showed. The study of the direction, time relations and magnitude of these currents constitutes modern electrocardiography.

APPARATUS

The instrument that is described in the present chapter is known as the "string galvanometer," the invention of the late Professor Einthoven. It consists essentially of a powerful electro-magnet, the poles of which are closely approximated (Fig. 1), and of an extremely delicate conducting fibre of silvered quartz or glass stretched in the narrow gap between the two magnetic poles. If minute currents are led through this fibre as it lies in the magnetic

field, the fibre moves across the gap in response to the tested current in a plane at right angles to the lines of magnetic force The magnified shadow of the fibre is vertical and is projected by means of an optical system and powerful light on to the horizontal slit of a camera the shadow moves at right angles to and across the slit and the movements are

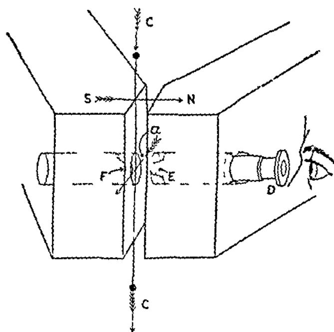


Fig 1 A diagram illustrating the construction of the string galvanometer The poles of the magnet (N S) are seen in outline the recording fibre (C C) lies vertically between them its movements may be observed through a microscope (D E) The movements of the string are in a plane parallel to the faces of the magnet poles as indicated by the central arrow (*a*) F is a condenser

photographed upon a sensitive plate that travels behind the slit I do not propose to describe in detail the construction of the galvanometer itself or of the accessory apparatus that is usually employed in obtaining human electrocardiograms Many different installations are now sold and some are specially arranged for clinical purposes The galvanometer

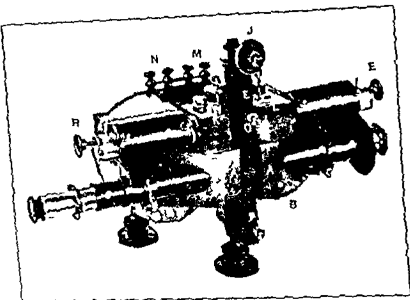


Fig (× }) A string galvanometer A A are the poles of the magnet B B the coils and H N the terminals carrying current to these D receives and condenses the beam of light upon the string which lies in the *string carrier (E)* the *microscope (C)* projects the image of the string on to the camera R and F are focussing screws The string carrier is pivoted on knife edges at K and L Current is led to the string through terminal O and I The string tension is adjusted by the screw J Carriers holding one string or two may be used

illustrated in Fig 2 is perhaps as serviceable as any and is to be recommended for the simplicity of its construction and the ease with which it is kept in order and manipulated The adjustments are simple and consist of mill headed screws which level the instrument centre the fibre in the field increase or decrease its tension and focus its shadow upon the camera Those who desire a more detailed account of the apparatus may refer to the special descriptions issued by its makers or to my book *The Mechanism and Graphic Registration of the Heart Beat* but familiarity with galvano

metric outfits can be gained best by handling the instruments I recommend the use of a galvanometer which is sufficiently sensitive without interposing amplification in any form

The galvanometer is connected to the patient through some special form of switchboard Students of electro cardiography utilise switchboards of different patterns more

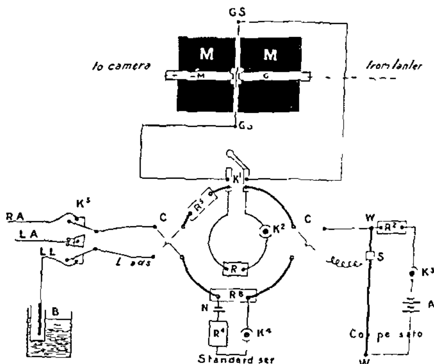


Fig 3 A switchboard arranged as a group of simple circuits and connected to the galvanometer

or less complicated those supplied for clinical use are arranged to insure speedy and accurate work the actual switches are therefore few in number but the wiring is intricate I *propose to describe a scheme that may be drawn as a* group of simple circuits This scheme though serviceable is no longer in clinical use because the number of the keys makes the manipulation of the board relatively slow But

I retain it as an illustration because its circuits and their use are easy to understand and because more complex board are arranged on similar principles

Fig 3 is a diagram of the apparatus and its connections The string of the galvanometer (*C S*) is connected to a key (K^1) which closes the string circuit The closure of this key brings the string to rest and safeguards it from damage The same key communicates with two circuits the inner and outer circles of the diagram the former is a shunt containing a resistance and key (R^1 and K^2) so arranged that when closed it carries the greater part of the tested current thus preserving the string from mishap It is used when a current of unknown strength is thrown into the string circuit The outer circle represents the main circuit it is broken at three points (1) at K^1 where it joins the string circuit (2) at C^1 by a commutator where it connects to the patient and (3) at C by a commutator where it connects to the compensator It contains also a dial resistance (*I*) and the standardiser The separate parts of the apparatus may be described briefly

Connection of patient

A wire that runs from the commutator C^1 to the key *K* may be connected at will to the right arm (*R A*) or left arm (*L A*) by means of the special key a second or parallel wire may be connected to the left arm or left leg (*L L*) by the same key The wires can be of any length though the shorter they are the less is the chance of interference by extraneous current The actual contacts may be made by immersing the limbs in salt water and through porous pots containing zinc sulphate and zinc rods (as indicated in Fig 3 *B*) Another and more convenient form of electrode which also shows no polarisation consists of a german silver plate strapped by a

subjects so essential to a proper understanding of this all important segment of dermatologic diagnosis and management

We shall therefore present a few comments on some aspects of melanin pigmentation, the melanocyte, the histogenesis and evolution of cellular nevi and on the limitations regarding correlation of clinical and pathologic features

BIOCHEMISTRY AND HISTOCHEMISTRY OF PIGMENTATION

Any discussion of the basic processes of pigmentation of the skin must begin with the fundamental work of Bruno Bloch[7] who in 1927 first showed by histochemical methods that the melanin pigment of the skin was formed through a process of enzymatic oxidation[6, 7] In a series of ingenious experiments using tissue sections incubated in a substrate of the naturally occurring amino acid 3 4 dihydroxyphenylalanine (DOPA) he demonstrated that specialized cells in the basal layer of the epidermis then referred to as melanoblasts (now known as melanocytes*) form melanin pigment Further it was concluded by Bloch that the DOPA oxidase contained in the melanocytes of human skin acted as a catalyst in the oxidation of DOPA to melanin

It was then shown that with the addition of plant tyrosinase DOPA was the first product formed in the enzymatic oxidation of tyrosinase to melanin Raper demonstrated that insect tyrosinase possessed both tyrosinase and DOPA oxidase activity[9] In 1950 Fitzpatrick Becker Jr Lerner and Montgomery[7] demonstrated the presence of tyrosinase activity in human skin In view of the distinct similarities between tyrosinase and DOPA oxidase they recommended that the term tyrosinase be used to denote the specific enzymatic activity instead of the separate terms tyrosinase and DOPA oxidase They were able to show that in human skin tyrosinase may exist in an inactive or partially inactive state providing the skin has not been irradiated with ultraviolet light Tyrosine can act as a precursor of melanin in human skin if the enzyme tyrosinase is activated by exposure to

* At the Third Conference on the Biology of [illegible] Atypical Cells [illegible] held in New York in 1951 a uniform [illegible] was adopted [illegible] embryonic cell with the potential to produce melanin [illegible] produces as well as contains melanin Melanophore [illegible] melanin is conf[illegible]

incidence of junction and intradermal nevi in the various groups is well known and the fact that it occurs is important for several reasons (1) as an aid in diagnosis (2) as an indication that junction nevi undergo changes with increasing age which manifest themselves histopathologically by a "dropping" (Unna) of the nevus cell from the epidermodermal junction into the cutis to become first compound nevi (i e nevi which histologically show a combination of junction and intradermal elements) and later become pure intradermal nevi (when junctional elements generally are no longer found and the nevus cells are in the dermis)[4,7]

Spitz[8] pointed out that 98% of the nevi of children studied by her showed junctional changes whereas these changes were noted by Allen in only 12% of the pigmented nevi of adults Similarly Stegmaier and Montgomery[29] found that 100% of the nevi of children showed junctional changes whereas Montgomery and Kernohan[30] noted that only 25% did so in adults These observations support the opinion that junction nevi tend to become intradermal with increasing age

Nevi which have junctional elements that is the junction nevi and compound nevi are generally accepted as being potential precursors of malignant melanoma[3, 4] According to Van Scott it is in the middle and late periods of adulthood when there are fewer pure junction nevi and a greater proportion of nevi with intradermal elements that the incidence of malignant melanoma is highest

The question naturally arises as to why the incidence of malignant melanoma is exceedingly low in childhood and relatively high in adulthood when the incidence of junction nevi is so high in childhood and relatively so low in adulthood (with the transition apparently taking place in the intervening years) As Traub pointed out in his discussion to Shaffer's paper[31] Whoever discovers the motivating factor (1) in bringing about junctional activity in the first place (2) in explaining why it goes to its logical conclusion as an intradermal process in some cases and is incomplete or entirely abortive in others and (3) what makes junctional activity fortunately quite rarely go on in some cases at some stage to true malignant activity can write the concluding chapter on this fascinating subject The same problem is discussed by

showed greater tyrosinase activity and therefore increased pigment in the more malignant and progressive tumors The count was high also in one case of ulcerated and infected prickle cell epithelioma this they attribute possibly to some bacteria capable of metabolizing tyrosine (using it as a nitrogen source)

Becker Jr Fitzpatrick and Montgomery[14] demonstrated that in specimens of normal vitiliginous and albino skin the number of melanocytes was constant and concluded therefore that the lack of pigmentation must be the result of variation in the function rather than in the number of cells present

We concur with the hopes previously expressed by others that knowledge of this difference between the enzyme systems of the cells of benign pigmented nevi and the cells of malignant melanoma may eventually contribute to the understanding of the genesis of malignant melanoma and aid in the in vivo diagnosis of this tumor

HISTOGENESIS OF NEVI

Much controversy still rages regarding the histogenesis of nevus cells and in turn the cellular nevi of man Suffice it to say that there are three theories as to their origin (1) that they are derived from melanocytes which are of neuroectodermal origin and are derived from the neural crest[1 19] (2) that they are derived from epidermal cells[0 21] (3) that they are of double origin a theory for which Masson[7] is the major proponent he suggested that the superficial portion originates in the cellules claires or melanocytes in the basal cell layer of the epidermis and that the deeper portion originates from the Schwannian nerve cells It would seem that the concept of the neurectodermal origin has the largest group of supporters today

THE EVOLUTION (PATHOGENESIS) OF CELLULAR NEVI

Traub and Keil[3] pointed out that pigmented nevi with the exception of bathing trunk nevi are usually not present at birth Junction nevi are frequent in the first two decades but become less so with advancing age Intradermal nevi are relatively less frequent in infancy but become more common in the young adolescent and in later years This difference in

clinical characteristics of these 45 pigmented lesions were of no aid in foretelling the histopathologic diagnosis

CORRELATION OF CLINICAL AND HISTOPATHOLOGIC FEATURES

In view of the gaps in our knowledge of the histogenesis and evolution of cellular nevi (nevus cell nevi*) it is not surprising that there is much controversy and confusion about the clinical classification and diagnosis of pigmented nevi On the basis of what is known about the evolution of cellular nevi it is best to distinguish between three clinical varieties (1) junction nevus (2) compound nevus and (3) intradermal nevus These three varieties are of utmost clinical importance because of the relative frequency with which they occur in various age groups the difficulties which arise in their differential diagnosis and the fact that malignant melanoma often appears to have its origin in junction and compound nevi and not in the intradermal variety

According to Becker Sr[33] cellular nevi are macular and usually not more than a few millimeters in diameter in the first 4 years of life after 10 years half of them have become elevated and may vary in size up to several centimeters Macular lesions are usually considered to be of more or less recent origin while the elevated ones which may be bearing hair are usually considered to have been present longer Of course exceptions would be the older but still flat lesions on the mucous membranes and palms and soles

As an aid in the clinical classification and recognition of these nevi as well as the others which we will discuss the classification of pigmented lesions by Shaffer[31] which is based on clinical criteria is worthy of presentation and consideration He attempted to carefully correlate the surface morphology of the various types of pigmented nevi (which he prefers to call melanocytic nevi) with their histopathologic appearance For purposes of analysis he divided the lesions clinically into the following categories

1 *Flat lesions* These are macular pigmented spots plain or speckled

2 *Slightly elevated lesions* These stand between flat and definitely elevated lesions They give the palpating finger a

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* W p f th term vu ci ll ev A sed b t ef t thos le s which h among th h t p th l g f t vu ll

Van Scott[3] who writes "If the assumption is made that intradermal nevi transitionally develop from junction nevi as available evidence would indicate then the consideration that melanomas develop from junction nevi at a time when such nevi undergo transition to intradermal type cannot be avoided The inferred corollary of this may be that the true precursor lesion of melanoma more specifically defined is the junction nevus in transition to the intradermal type in which there is interference with this process Further studies concerning the normal benign invasion of the dermis by epidermis nevus cells during the transition of junction nevi to intradermal nevi would seem to be helpful in a better understanding of the pathogenesis of malignant melanoma

INCIDENCE OF PIGMENTED NEVI

The incidence of pigmented nevi differs greatly according to different authors According to Pack and Davis[77] *2 4% of 200 infants presented pigmented nevi* while Kissmeyer[84] noted that they were present in 35% of newborn infants

Siemens[3] recorded an average of 30 nevi per adult person In an examination of 1 000 adult white patients Pack *et al*[36] counted *a total of 14 609 nevi or an average of 14 6 per person* No person was free of nevi Of these 14 609 nevi 13 2% occurred on the head and neck 0 1% on the genitalia 30 2% the upper extremities *30 3% on the trunk and 17 1%* on the *lower extremities Interestingly they found nevi on the* palms and soles in only 5 instances or 0 034% This extremely low *incidence* of nevi on the palms and soles differs considerably from the report of Lerner[3] who observed that approximately *10% of* college students had nevi on these areas and the more recent observations of Van Scott Reinertson and McCall[3] who found that 25% of persons examined presented at least one such lesion These authors found *that* pigmented nevi rarely *occur on* palms and soles of children as compared with people in the 2d 3d and 4th decades Forty five of these pigmented lesions were excised from 40 of the adult patients and were examined histopathologically Seven were diagnosed as *lentigo* 15 as junction nevi 15 as compound nevi and 1 as an intradermal nevus The remaining 7 showed only hyperpigmentation in the basal layer The

ical diagnosis was incorrect in 26% Investigations by Becker Sr[41] revealed a somewhat more encouraging picture in a clinic where dermatologists and graduate students in dermatology made the clinical diagnosis of pigmented nevus The diagnosis was confirmed histopathologically in 80% of 710 lesions and where the microscopic diagnosis of pigmented nevi was made the clinical diagnosis had been correct in 87% of 649 lesions

EPHELIS (FRECKLE)

Ephelides are light tan to dark brown macules which vary in size from 1 to several millimeters in diameter They are usually multiple varying from a few in number to hundreds or thousands and while usually discrete they may be grouped or confluent They are found predominantly on the exposed parts of the body as the face shoulders and upper back forearms and dorsum of hands they are infrequent on the palms and soles They are more noticeable in persons with red hair and fair complexion

Ephelides may appear early in life although they are usually not seen before 6-8 years of age They usually increase in number over the years and tend to persist some characteristically become more prominent following exposure to the sun and other causes of increased pigmentation others fade so as to almost disappear with the absence of exposure to the sun

Ephelides derive their color from the collection of melanin pigment in the basal cell layer in dopa negative cells nevus cells are not seen These lesions remain benign and need not be treated except for cosmetic reasons where desired

Isolated lesions may be treated by local application of a solid carbon dioxide pencil shaped to the size of the lesion The pencil is held in place with moderate pressure for 5 10 seconds This is followed by erythema and slight edema sometimes a vesicle forms The treated site then becomes darker and somewhat scaly and in about 7 10 days when the brownish crust or scale peels away a slightly pink spot is seen which gradually takes on the color of the surrounding skin

Ephelides should be differentiated from lentigines flat

slight feeling of thickness and sometimes are slightly raised above the surrounding skin

'3 *Halos* These are elevated lesions each of which is surrounded by a pigmented macular ring

4 *Verrucoid lesions* These are pigmented lesions covered with fine digitate excrescences

'5 *Polypoid lesions* The surface of these lesions consists of coarse club tipped protuberances

6 *Dome shaped lesions* These rise smoothly from the level of the surrounding skin to form a mound like elevation

'7 *Sessile lesions* These are smooth surfaced lesions arising sharply from the surrounding skin with a slightly constricted base

'8 *Pigmented papillomas (pedunculated lesions)* These are pigmented lesions attached to the skin by means of a stalk or a pedicle

Histopathologic examination of these 8 clinical varieties led to the following inferences group 1 lesions were almost always junction nevi groups 2 and 3 were made up of compound nevi largely group 4 consisted of intradermal nevi primarily with some evidence of junctional activity groups 5 6 7 and 8 were almost consistently intradermal nevi For details of the clinical and pathologic relationships of these lesions the reader is referred to Shaffer's original articles[31, 39] We wish to stress however that the clinical diagnosis of these nevi should not be based exclusively on the findings set forth by Shaffer who was careful to caution concerning this himself We suggest that *all* the clinical features time of onset location of the lesion as well as the age of the patient etc be taken into consideration when attempting to establish the diagnosis Unless this is done the correct clinical diagnosis will often be missed Unfortunately not many studies have been reported concerning the percentage of cases in which the clinical diagnosis was corroborated by histopathologic study Those studies which have been published however reveal a somewhat frightening situation Of 561 lesions on which the clinical diagnosis of pigmented nevus was made by nondermatologists Swerdlow[40] reported a microscopic diagnosis which showed that they were in error in 39% of the cases Of 454 specimens for which a histopathologic diagnosis of pigmented nevus was made the clin

ical diagnosis was incorrect in 26%. Investigations by Becker Sr[11] revealed a somewhat more encouraging picture in a clinic where dermatologists and graduate students in dermatology made the clinical diagnosis of pigmented nevus. The diagnosis was confirmed histopathologically in 80% of 710 lesions and where the microscopic diagnosis of pigmented nevus was made the clinical diagnosis had been correct in 87% of 649 lesions.

EPHELIS (FRECKLE)

Ephelides are light tan to dark brown macules which vary in size from 1 to several millimeters in diameter. They are usually multiple, varying from a few in number to hundreds or thousands, and while usually discrete they may be grouped or confluent. They are found predominantly on the exposed parts of the body, as the face, shoulders and upper back, forearms and dorsum of hands; they are infrequent on the palms and soles. They are more noticeable in persons with red hair and fair complexion.

Ephelides may appear early in life, although they are usually not seen before 6-8 years of age. They usually increase in number over the years and tend to persist; some characteristically become more prominent following exposure to the sun and other causes of increased pigmentation; others fade so as to almost disappear with the absence of exposure to the sun.

Ephelides derive their color from the collection of melanin pigment in the basal cell layer in dopa-negative cells; nevus cells are not seen. These lesions remain benign and need not be treated except for cosmetic reasons where desired.

Isolated lesions may be treated by local application of a solid carbon dioxide pencil shaped to the size of the lesion. The pencil is held in place with moderate pressure for 5-10 seconds. This is followed by erythema and slight edema; sometimes a vesicle forms. The treated site then becomes darker and somewhat scaly and in about 7-10 days, when the brownish crust or scale peels away, a slightly pink spot is seen which gradually takes on the color of the surrounding skin.

Ephelides should be differentiated from lentigines, flat

junction and compound nevi and pigmented spots associated with conditions such as incontinentia pigmenti and Jeghers Peutz syndrome

LENTIGO (LENTIGINES)

Unfortunately the term lentigo which is so frequently used has different connotations to different dermatologists to the extent that the term is proving confusing We would therefore like to review briefly *some of the lesions for which* the term is used Lever[57] states that histopathologically lentigo is represented by elongation of the rete pegs which also appear club shaped The basal cell layer shows increased pigmentation and an increase in the number of clear cells The dopa reaction is positive No junction components are noted Shaffer[31] however refers to lentigo as an inactive junction nevus—in other words a potential junction nevus without evidence of junctional activity '

Becker Sr[1] used the term lentigo maligna as follows lentigo meaning an acquired brown macule and maligna denoting the ominous nature of the process I believe that lentigo maligna is an obligative premalignant (or malignant) lesion (i e for malignant melanoma —Eds)

We are of the opinion that in order to avoid confusion it is best to adhere to Lever s definition and use the term *lentigo* or *simple lentigo* to apply only to the lesion clinically described below which does *not* possess nevus cells or junctional elements

Lentigines ordinarily are medium to dark brown sometimes with a blackish hue and vary in size from approximately 1 millimeter to several millimeters in diameter They are macules or *very slightly elevated papules and are irregularly* round or oval in configuration They appear singly or in great numbers and are usually discrete and isolated They may appear *anywhere on the body* surface although they are most common on the genitalia thighs and trunk In the aged the lesions are more frequent on the dorsa of the hands the forearms and the face (lentigo senilis)

Lentigines may appear at any age although they usually develop early (within the first 3 years of life) ordinarily persist for years and generally remain unchanged Their pres

ence i not usually influenced by exposure to the sun al though ome may darken in color with prolonged exposure

Lentigines must be differentiated from ephelides junction and compound nevi and ometimes even early malignant melanoma There is yet another variety of lentigo referred to by Cawley and Curtis[4] as *lentigo senilis* (commonly called liver spots) These are pigmented lesions which are irreg ular in shape may reach the size of 1 cm or more in diameter vary in color from light to dark brown may be pre ent singly or in numbers and are located primarily on the dor a of the hands and wrists and less often on the face and ankles They are quite common occurring in 25 30% of persons over 50 years of age They rarely become malignant Their histologic chara teri tic include a moderate degree of acanthosis large cells in the stratum mucosum fairly numerous clear cells in the basal layer which i heavily pigmented and eccentric thumb like buds from the rete pegs The cells of these bud are trongly dopa positive Zones of atrophic dermis and bas ophilic degeneration are seen

Because of the benign nature of simple and senile lentigo they ordinarily do not have to be removed except for diagnos tic or c smetic purposes When they are small they can be exci ed easily with a scalpel thus affording a histopathologic diagno is and an acceptable cosmetic result The very light colored lesions may be destroyed either with solid carbon di oxide or by electrodesiccation and curettage

BLUE NEVUS (JADASSOHN TIECHE)

The blue nevu is usually dark blue but the shades may vary from light to dark including yellow brown gray light blue and even black The pigment while usually solid may be mottled The lesions vary in size from 1 to 2 mm to 1 cm and ometime larger in diameter They are usually firm and smooth slightly elevated to hemispherical and round to oval although they may have a slightly irregular configuration Blue nevi usually develop during infancy Ordinarily they remain unchanged and only one such lesion is found on any one per on although the appearance of several lesions is not unu ual The lesion are discrete and may be found anywhere

on the surface of the skin the greatest number occurring on the extremities and face

The color of the blue nevus is the result of the collections of melanin in the dendritic cells (melanocytes) in the cutis The pigment in these cells appears blue or blue black to the eye as the result of light being refracted through the superficial cutaneous tissues the color varies with the depth of the pigment in the cutis The blue nevus cells are dopa positive early in life but may later lose this activity especially in the deeper cells The origin of these cells—whether from the sheath of Schwann (Masson) or from melanocytes interrupted in their migration from the neural crest to the basal layer of the epidermis—remains in controversy

These lesions are benign and ordinarily need not be treated except for cosmetic reasons Because of their small size they are best removed by simple surgical excision with a 1 2 mm border of normal skin and primary closure In the extremely rare instances where malignancy has occurred the lesion usually has been found to be a cellular blue nevus i e a combination of blue nevus and cellular nevus The cellular blue nevus is usually larger and more elevated than the ordinary blue nevus

The blue nevus must be differentiated from hemangioma glomus tumor epithelial cysts intradermal and junction nevi and more often from malignant melanoma At times tattoos prove confusing in the differential diagnosis

INTRADERMAL NEVUS

Intradermal nevi vary in color from that of the skin to medium or dark brown Rather than always appearing solid in color on careful examination flecks of tan to brown pigment are sometimes seen The lesions vary in size from 1 to 2 mm to many centimeters although they are more commonly approximately ½ 1 cm in diameter They may or may not contain hairs These lesions are ordinarily elevated some are only slightly elevated while others are hemispherical sessile or pedunculated From one to many dozens may be located anywhere on the body surface although they are most common on the face While these lesions are rarely present at birth they often appear later in life most frequently during the adolescent or young adult years

Histopathologically the intradermal nevus is characterized by true nevus cells located in the cutis and separated from the basal layer

Treatment of these ordinarily benign lesions is not necessary except when they are located in areas subject to frequent trauma or irritation or for cosmetic reasons Numerous forms of treatment may be used all of which if properly applied afford a satisfactory cosmetic result These include desiccation and curettage superficial desiccation and curettage followed several weeks later by the local application of trichloroacetic acid the repeated application of trichloroacetic acid alone ablation of the lesion with scalpel followed by light desiccation of the base or ablation with scissors (by these latter methods a specimen may be procured for histopathologic study) and the repeated introduction of a fine needle and galvanic current through the base of the nevus in a crosshatched fashion Any of these methods should be used in such a manner that the lesion is flattened down to the level of the skin without attempting complete removal

When the intradermal nevus is hairy it is wise to first remove the hairs by electrolysis before attempting any other method for destruction of the nevus for when the hairs are removed first the nevus itself sometimes shrinks and therefore leaves less tissue to be destroyed As a matter of fact the depilation alone is sometimes sufficient to remove smaller hairy intradermal nevi and produces a most acceptable cosmetic result

Intradermal nevi must be differentiated from junction and compound nevi which they most closely resemble and less frequently from fibromas cutaneous nodules pigmented basal cell epitheliomas and seborrheic keratoses

COMPOUND NEVUS

The term compound nevus as previously pointed out refers to those lesions which histologically show both junction nevus cell elements and intradermally situated nevus cells Traub and Keil [3] referred to this type of lesion as combined or mixed nevus but it would seem that through common usage it has been replaced with the term compound nevus and that the terms combination nevus or mixed nevus

have come to mean a combination of a nevus cell nevus with some other entirely different variety of nevus

While compound nevi clinically have some of the features of the intradermal nevus they are usually more pigmented may be flatter and less well defined and thus are more likely to simulate the junction nevus They occur prepubertally and in later years According to Allen the chances of a compound nevus becoming malignant are very low Van Scott *et al* make the point that the incidence of malignant melanoma is

INDICATIONS FOR THE TREATMENT OF NEVUS CELL NEVI*

Treatment Mandatory

1 Those which have undergone changes or shown activity such as sudden enlargement bleeding inflammation alteration in color (either darker or lighter) ulceration crusting development of satellite pigmented areas or those which become symptomatic (especially pruritic or painful)
2 Those showing activity during pregnancy [43]
3 Those which histologically show evidence of unrest e g precancerous junction nevi [44]
4 Those in which the physician recognizes clinical features which suggest the presence of one of those closely related conditions which are known to undergo malignant transformation in a high percentage of instances (e g melanotic freckle of Hutchinson[45] and precancerous melanosis)[46]

Treatment Generally Considered Advisable

1 Nevus cell nevi at sites where the incidence of malignant melanoma is relatively high such as genitalia mucous membranes and subungual areas [38]
2 Juvenile melanomas [illegible]

Treatment Controversial

1 Those at sites of repeated trauma
2 Those appearing beyond the 2d decade of life
3 Those located on palms and particularly on soles (see text)

* From Witten V H and Kopf A W [illegible] nevi and skin cancers M Cl n North Amer [illegible]

highest apparently when the proportion of nevi with intradermal elements is greatest i e in those age group where transition from junction to intradermal nevus occurs with the greatest frequency In view of the differing statistics and varying conclusions this problem requires clarification

Compound nevi may be treated by any one of several methods provided therapy is necessary at all (see table) Where there is any doubt concerning the diagnosis scalpel excision with conservative borders is the treatment of choice (see Junction Nevus) where the pigment is confined to the um

mit of a hemispherical lesion it may be ablated with a scal pel (thus affording a biopsy specimen) and the base desic cated and curetted We do not favor cryotherapy e charotics or electrodesiccation of lesions suspected of being compound nevi they should be managed as above or left alone

JUNCTION NEVUS

In 1940 Traub and Keil while pre enting a cla sification of the pigmented nevi based on the microanatomic location of the lesions first used the term junction nevus and used the expression common mole to designate the intradermal nevus

Junction nevi vary in size from approximately 1 mm to many centimeters in diameter and in color from very light tan to dark brown (even black) It is not unusual for the pig mentation to be mottled in distribution Ordinarily junction nevi are flat or slightly elevated are well defined and may have the configuration of a small papule or a large hemi spherical nodule The surface of these lesions is usually smooth although it may become roughened Hairs (other than lanugo) are usually absent The number of lesions var ies from one to several dozens They usually occur singly anywhere on the body but in particular on the extremities and the face on the trunk they are most commonly located on the upper back and shoulders

Pigmented nevi of the palms and soles ordinarily are flat and are junction nevi In these locations they vary in size from a barely visible fleck of pigment to light tan to dark brown areas up to 1 cm or more in size Careful examination of these lesions will often reveal a speckling of the pigment at times appearing as small pseudopodia extending out into the apparently normal tissues

Junction nevi may appear at any age and may increase in size very slowly until they reach the average limits for this particular variety of nevus Histopathologically true nevus cells are found in theques (nests) in the basal cell layer to gether with clear cells in addition nevus cells are found in the uppermost cutis at the junction of epidermis and dermis

Ordinarily junction nevi remain benign but when malig nant melanoma does develop from a previously existing ne

vus it is usually a junction nevus or less often, a compound nevus Because of this possibility great concern and caution are voiced regarding the management of these particular nevi While there are some physicians usually nondermatologists, who recommend the surgical excision of *all* lesions suspected of being junction nevi, there are many reasons which speak strongly against this viewpoint

It is not unusual for patients to have been advised that such pigmented lesions be excised before puberty and early in pregnancy as the incidence of malignant transformation is apparently greater during puberty and gestation However just as it is impractical and illogical to excise all pigmented *lesions suspected of being junction nevi so is it illogical to* excise all those pigmented lesions present before puberty or during early pregnancy The indications for excision of pigmented lesions during these two periods of life remain the *same as the indications for the removal of any of the pig*mented lesions previously described

According to one group of investigators[32] ¼ of the individuals of our total population have one or more pigmented nevi on the palms and soles *the greatest percentage of these* lesions are junction nevi While there are some physicians who advocate surgical excision of *all* such lesions because of the possibility of their becoming malignant melanomas it is our opinion that such management is out of the question as is the removal of *all* pigmented nevi which occur elsewhere on the skin surface

Where lesions are clinically suspected of being junction nevi and when there are distinct *indications* for the removal of such lesions (see table) the treatment of choice is conservative surgical excision including about 1 or 2 mm of normal tissue at the periphery Such a procedure is carried out under local anesthesia and the wound is *closed* by sutures

Junction nevi must be differentiated from intradermal nevi compound nevi malignant melanomas lentigines cutaneous nodules *blue nevus, tattoos cafe au lait spots etc*

BENIGN JUVENILE MELANOMA
(JUVENILE MELANOMA, PREPUBERTAL MELANOMA)

Of all the pigmented lesions occurring in young people none is more important *in differential* diagnosis nor more

misunderstood than the one referred to as juvenile melanoma a term coined by Spitz The difficulty in establishing the diagnosis of the lesion based on gross morphologic appearance is the result of there being no absolutely characteristic clinical picture In addition the histopathologic picture of benign juvenile melanoma is often confused with that of malignant melanoma of adults It is obvious that it is extremely important to be able to recognize benign juvenile melanoma and to differentiate it from malignant melanoma since the clinical course of benign juvenile melanoma is benign in contradistinction to malignant melanoma from which one can anticipate a high percentage of metastases and eventual death

The very use of the word melanoma is in itself confusing as common usage has given the term the meaning of *malignant* melanoma and therefore interpretation by the uninitiated would lead to the erroneous conclusion that a (benign) juvenile melanoma* is a malignant melanoma occurring before the onset of puberty As we shall attempt to point out this is *not* the case as there are certain clinical and histologic characteristics which help to differentiate the benign juvenile melanoma from the *malignant melanoma which in exceptional instances also may occur in prepubertal years*

The benign juvenile melanoma is often difficult to recognize and therefore the clinical diagnosis ordinarily would not be suspected except by specially trained and experienced dermatologists or other physicians Nevertheless the clinical features of benign juvenile melanoma may be of some help in making the diagnosis Benign juvenile melanomas vary in color usually from pink to red although they may bear pigment from brown to black Ordinarily by the time they are called to the physician s attention they are approximately 1 cm in size although they may be larger They are round or oval occasionally have irregular borders are sharply defined and elevated are usually quite smooth but may be rough or verrucous at the surface Dark coarse hairs are not ordinarily seen

Benign juvenile melanomas can occur on any part of the

If f rth pen hould onfirm th ben gn at f j l m la m w would t gly n m f th s l on wh ch would not lud th word m l om U t] h t m w p f th t rm be n j en l m l m lso sed by Sp tz d Allen w ll by M Wh rt nd W ol

body but seemingly are more common on the face and extremities—in particular the lower extremities They may be present at birth or develop anytime thereafter but usually within the first 3 years They usually grow slowly and it may be difficult to decide whether the growth is in proportion with the child's growth or greater Lesions with these clinical characteristics which also have the accepted histopathologic picture of benign juvenile melanoma described by Spitz and Allen as a rule remain benign It is obvious therefore, that the final diagnosis depends on the correct interpretation of the histopathologic changes

The incidence of true malignant melanoma (melanocarcinoma) in childhood has been stated by Allen to be in the vicinity of 0 3% of all melanocarcinomas of the skin and mucous membranes On the other hand the incidence of benign juvenile melanoma is quite high when compared with ordinary benign nevi occurring in children according to Spitz the ratio is approximately 1 12 However it should be taken into consideration that this ratio may well be greatly biased in favor of benign juvenile melanomas since only highly selected nevi are ordinarily removed during childhood The ultimate outcome of untreated benign juvenile melanomas for the time being remains unknown but when one considers their apparently significant incidence in childhood and the very low incidence of melanocarcinoma in childhood then one is justified in assuming that their course is essentially a benign one during this period of life

The incidence of benign juvenile melanomas drops sharply after puberty and they are rare after the 3d decade It is assumed therefore that benign juvenile melanoma may acquire the histologic characteristics of intradermal nevi after puberty If all the evidence which has been accumulated to date indicating the benign character of benign juvenile melanomas is correct then treatment need be conservative only consisting of surgical excision with a margin of a few millimeters There is no need for wide and deep radical surgery

It is not our intention here to set forth in detail the histopathologic criteria for the diagnosis of benign juvenile melanoma We do however side with those authors who agree with the opinions of Spitz [3] and Allen [4] that the diagnosis of this melanoma can be made by experienced pathologists

through recognition of certain histopathologic features

The cytologic features of benign juvenile melanoma as described in 1948 by Spitz include (1) the relative superficiality of the essential landmarks of the lesion (2) the two elements of a compound nevus junctional and intradermal (3) edema and telangiectasia of the cutis just below the epidermis (4) the tendency for single cells or compact nests of spherical or spindle cells to be segregated sharply from the adjacent ones (5) the occurrence of large cells with abundant usually uniformly basophilic myogenous appearing cytoplasm (6) the superficially located characteristic giant cells those with the single large nucleus as well as the multinucleated ones resembling the pattern either of the giant cells of measles or Touton giant cells with a complete or incomplete peripheral rim of small nuclei (7) the generally abrupt transition between the acantholytic loose junctional cells and the still intact adjacent epidermis and (8) the relative sparsity of pigmentation so that in association with the superficial dermal edema and telangiectasis most of the juvenile melanomas clinically appear purplish red rather than dark brown In addition to this very distinctive coloration the juvenile melanomas tend to be hairless larger and more elevated than the usual nevus of childhood

On the basis of the histologic criteria just outlined it is possible in about two thirds of the cases to learn to differentiate the benign juvenile melanomas from the adult melanocarcinomas in the remainder this histologic differentiation is not possible without knowledge of the age of the patient However if the prepubertal age of the child is made available to the pathologist there then can be very little doubt that the lesion is benign if the exceptional patterns outlined in the following sections are borne in mind

There is some evidence that not only do benign juvenile melanomas become simple intradermal nevi after puberty but that a small percentage of melanocarcinomas in adults show some residual evidence of a pre existing benign juvenile melanoma The benign course of the benign juvenile melanoma diagnosed according to the clinical and histopathologic criteria outlined together with the much lesser incidence of these histopathologic findings in lesions studied after puberty all point to the justification for conservative management of

these essentially benign growths To perform *radical* surgical extirpation of every lesion having the clinical and histopathologic features of a benign juvenile melanoma would be comparable to amputating every breast with cystic mastitis simply because of the possibility that carcinoma might develop in these tissues in later years

The practical approach then to the management of any lesion which clinically is suggestive of a benign juvenile melanoma would be simple surgical excision including only several millimeters of normal appearing surrounding skin Because of the small size of these lesions the wound usually can be closed easily by suture to heal by primary intention This procedure then allows for accurate histologic diagnosis provided the specimen is sent to a pathologist who is especially well trained in the field of dermatologic histopathology We are stressing this fact because it has been our experience repeatedly that the same specimen which is correctly diagnosed by the specially trained dermatopathologist as a benign juvenile melanoma is often interpreted as a malignant melanoma by highly competent general pathologists The procedure of simple excision with a narrow border of normal skin also completely eliminates such lesions as a source of possible future difficulty This is of potential importance in case further studies in this field should suggest that remnants of benign juvenile melanomas later in life may become the source of true malignant melanoma

GENERAL REMARKS REGARDING MANAGEMENT

Rather than review the various statistics indicating what percentage of malignant melanomas originate from junction or compound nevi it seems to us more important to point out that it is estimated that only one out of a million or more pigmented nevi becomes malignant [48] Considering that the average person has approximately 20 nevi this would mean that 1 person in 50 000 can be expected to develop a malignant melanoma from clinically evident pigmented lesions The phrase clinically evident pigmented lesions is intentionally used as apparently *a large percentage of malignant melanomas have their origin at sites clinically free of existing nevi*

As discussed elsewhere we agree with those who feel that each nevus must be individually evaluated and that the decision as to whether or not it should be removed and the method to be used should be based on consideration of all factors[49]

After the decision has been made to remove given lesions in general those diagnosed as junction or compound nevi or as benign juvenile melanomas should be surgically excised with a narrow border Elevated dome shaped sessile pedunculated and polypoid lesions may often be snipped off at the base which in turn is electrodesiccated

Pigmented lesions such as ephelides simple lentigo senile lentigo and intradermal nevi as has been pointed out may be destroyed by a number of means including the application of trichloroacetic acid carbon dioxide pencil electrodesiccation etc When any of these methods are used for cosmetic reasons efforts should be made to destroy all of the areas of pigmentation There are undoubtedly many hundreds of thousands and perhaps millions of lesions some of which are almost certainly junction nevi which are destroyed by one or more of these means every year And we know of no properly documented evidence where histologically verified benign pigmented lesions were stimulated to become malignant melanomas as a result of burning the surface cutting through the lesion or other local traumatic exercises Of course when the diagnosis is in question a specimen should always be taken for histopathologic examination Should the result of microscopic study suggest possible malignant transformation then the remaining area plus an area of normal appearing surrounding skin can be surgically excised

A great controversy has surrounded the question concerning whether a lesion suspected of being malignant melanoma might be cut into for the purpose of obtaining tissue for microscopic study or if such a lesion initially should be totally excised widely and deeply While it is difficult to establish definite criteria which apply in all cases we are of the opinion that where there is serious doubt that the lesion is a malignant melanoma with rare exceptions it should be excised in toto with allowance only for a *small border* of clinically normal tissue Additional surgery can always be carried out if the diagnosis of malignant melanoma is histologically con

firmed This procedure helps to avoid unnecessary cutting into the lesion as well as unnecessarily extensive surgery

A decision regarding the management of lesions which are *highly suspected* of being malignant melanoma can be made only after consideration of *all* of the factors involved and such decisions should be made only by experts in this particular field preferably a team consisting of a dermatologist and a "tumor surgeon

CONCLUSIONS

The clinical and histopathologic features of selected benign cutaneous pigmented lesions and their management have been reviewed These lesions are among the most important cutaneous problems with which the practitioner is confronted They are also among the most common particularly in recent years because of the publicity which has surrounded 'pigmented moles'

While the vast majority of these pigmented lesions remain benign one in many millions eventually undergoes malignant changes Therefore it is essential from both the prognostic and therapeutic viewpoints that one should know which particular varieties of these lesions do and do not possess such malignant potentialities

In most instances the well trained clinician can establish a diagnosis on the basis of clinical examination and the history In doubtful cases a histologic examination preferably by a pathologist who has had special training and experience in the diagnosis of pigmented lesions is an absolute necessity Only in this manner is it feasible to avoid potentially serious mistakes

A continuing search must be carried on for biochemical or other in vivo methods which will permit differentiation between benign and premalignant or malignant pigmented lesions

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I TREATMENT AND PREVENTION

A Local Drug Therapy

Treatment of Dermatoses with Local Application of Triamcinolone Acetonide New Synthetic Corticoid Preliminary Report is presented by Raymond C V Robinson[1] In a pilot study on 35 patients using the double blind paired comparison method the anti inflammatory action of 0.1% triamcinolone acetonide lotion was found to be similar to that of lotions containing 0.1% fludrocortisone or 1% hydrocortisone In 40 patients with inflammatory dermatoses 0.1% triamcinolone acetonide in water miscible base was at least as effective as 1% hydrocortisone in the same water miscible base

Satisfactory results were obtained in the treatment of 74 of 76 patients with atopic dermatitis 31 of 32 with seborrheic dermatitis 38 of 40 with contact dermatitis 17 of 17 patients with localized neurodermatitis 8 of 9 with pruritus ani and 7 of 8 with pruritus vulvae using 0.1% triamcinolone acetonide ointment or lotion There was no significant effect on psoriasis lesions As with other locally applied corticoids flare ups occurred after discontinuance of local applications of triamcinolone Relief was maintained however for the duration of treatment and it was usually possible to lessen the frequency of applications as symptoms subsided

Six patients with Candida albicans paronychia and 16 with C albicans infections of the genitocrural region were treated with a cream containing 0.1% triamcinolone acetonide and 100 000 units of nystatin 2.5 mg neomycin sulfate and 0.25 mg Gramicidin/Gm 3 with paronychia and 14 with crural moniliasis were improved

Triamcinolone Acetonide Highly Effective New Topical Steroid has an anti inflammatory effect in animals 40 times as great as cortisone or hydrocortisone In a double blind study J Graham Smith Jr Raymond J Zawisza and Harvey Blank[2] (Univ of Miami) compared 0.1% triamcinolone ace

(1) Bull School Med Univ Maryland 43 54-57 July 1958
(2) AMA Arch Dermat 78 643-645 November 1958

tonide with 1% hydrocortisone as used topically in lotion cream and ointment bases in 109 patients with inflammatory skin diseases After treatment for 1 week to 1 month or longer each patient was asked to evaluate the preparations The examining physician also made an evaluation of the sites of application for objective evidence of difference in effectiveness

In 75 patients (68 7%) 0 1% triamcinolone acetonide was more effective subjectively and objectively than 1% hydrocortisone In 27 patients the drugs were equally effective subjectively and in 28 patients were equally effective objectively In only 4 patients (3 7%) was there subjective evidence of superiority of hydrocortisone and in 3 (2 8%) *objective evidence* Patients who had been treated unsuccessfully with many other topical steroids showed for the first time complete regression of lesions after treatment with triamcinolone acetonide Body weight of several patients was *followed but there was no gain or loss After extensive local* use of 30 ml of 0 1% triamcinolone acetonide daily for 6 days in 1 patient no changes occurred in chloride sodium and potassium serum electrolytes or in body weight No case of sensitivity was observed

► [In our own experience triamcinolone acetonide is proving to be the most effective topical corticosteroid yet to be introduced We know of no reports of systemic absorption and undesirable side effects from the continued and widespread use of this compound It is particularly interesting that when given orally the acetonide is no more effective than triamcinolone free alcohol —Eds]

Experimental and Clinical Evaluation of New Hydrocortisone Derivative (Hydrocortisone 21 Xanthogen Ethanolamine) for Topical Use H Haxthausen[3] (Univ of Copenhagen) *observes that the hydrocortisone derivative is hy*drolyzed in the presence of water It is relatively stable in a mixture of 1 part lanolin and 9 parts petrolatum but even here 20% decomposition occurs in 2 months of refrigeration

By use of the electrophoretic patch test 1 3 c hydrocortisone 21 xanthogen ethanolamine (corresponding to 1% hydrocortisone after hydrolysis) 1% 9α fluorohydrocortisone and 1% hydrocortisone acetate were compared in 20 experiments Each substance was used in a base consisting of 1 part lanolin and 9 parts petrolatum and the base itself was

(3) Acta derm venereol 3 435-439 195

u ed as a control Strong to complete inhibition of the eczem atous reaction resulting from electrophoresis occurred in 3 instances with hydrocortisone 21 xanthogen ethanolamine and in 2 instances with fluorohydrocortisone Weak to mod erate inhibition occurred in 10 experiments with the new substance 5 with hydrocortisone acetate 9 with fluorohy drocortisone and 1 with the control The results indicate that hydrocortisone 21 xanthogen ethanolamine is about as ef fective as fluorohydrocortisone when applied topically for the purpose of inhibiting experimental eczema

In clinical trials the new derivative was used in an ointment base made by mixing equal parts of two ointments (1) hy drocortisone xanthogenic acid in petrolatum and (2) eth anolamine in petrolatum 42 5% mono-olein 2 5% lanolin 5% and water 50% The effectiveness of this mixture con taining 1% hydrocortisone 21 xanthogen ethanolamine was compared with that of a commercial ointment containing 1% hydrocortisone acetate in 81 cases of eczema and 38 of atopic dermatitis The new derivative was more effective in 42 instances hydrocortisone acetate was more effective in 12 in tances and there was no difference in 66 The author con cludes that the clinical effectiveness of the new preparation i somewhat greater than that of hydrocortisone acetate and is apparently about equal to that of fluorohydrocortisone It is much less apt to produce general effects when absorbed locally however since it is broken down to hydrocortisone which is much less active than fluorohydrocortisone The problem of stability of hydrocortisone 21 xanthogen etha nolamine has been solved by dispensing the preparation in a special double tube the xanthogen and ethanolamine com ponents to be mixed before application

► [New corticosteroid compounds for topical application continue to be come availabl We *have no* personal experience with the particular com pound tested by Haxthausen Of the newer compounds which we have e aluated t iamcinolone acetonide has been *the most* promising I ated con par son te ts in many instances showed a 0 1% concentration of this sub tance to be somewhat more effective than 1% hydrocortisone 0 2% t amci olone *acetonide* in turn appeared somewhat more effective than 0 1% in m st ca es Whether the topical effectiveness of this compound can be augmented by increasi g its concentration remained unanswered as loes the quest on What is the optimal concentration from the economic vi wpoint

Perhaps the day *is not* far off when the pharmaceutical industry will develop cortico tero d compoun ls for topical appl cation which will hav

tonide with 1% hydrocortisone is used topically in lotion cream and ointment bases in 109 patients with inflammatory skin diseases After treatment for 1 week to 1 month or longer each patient was asked to evaluate the preparations The examining physician also made an evaluation of the sites of application for objective evidence of difference in effectiveness

In 75 patients (68 7%) 0 1% triamcinolone acetonide was more effective subjectively and objectively than 1% hydrocortisone In 27 patients the drugs were equally effective subjectively and in 28 patients were equally effective objectively In only 4 patients (3 7%) was there subjective evidence of superiority of hydrocortisone and in 3 (2 8%) objective evidence Patients who had been treated unsuccessfully with many other topical steroids showed for the first time complete regression of lesions after treatment with triamcinolone acetonide Body weight of several patients was followed but there was no gain or loss After extensive local use of 30 ml of 0 1% triamcinolone acetonide daily for 6 days in 1 patient, no changes occurred in chloride sodium and potassium serum electrolytes or in body weight No case of sensitivity was observed

► [In our own experience triamcinolone acetonide is proving to be the most effective topical corticosteroid yet to be introduced We know of no reports of systemic absorption and undesirable side effects from the continued and widespread use of this compound It is particularly interesting that when given orally the acetonide is no more effective than triamcinolone free alcohol —Eds]

Experimental and Clinical Evaluation of New Hydrocortisone Derivative (Hydrocortisone 21 Xanthogen Ethanolamine) for Topical Use H Hasthausen[1] (Univ of Copenhagen) observes that this hydrocortisone derivative is hydrolyzed in the presence of water It is relatively stable in a mixture of 1 part lanolin and 9 parts petrolatum but even here 20% decomposition occurs in 2 months of refrigeration

By use of the electrophoretic patch test 1 3% hydrocortisone 21-xanthogen ethanolamine (corresponding to 1% hydrocortisone after hydrolysis) 1% 9α fluorohydrocortisone and 1% hydrocortisone acetate were compared in 20 experiments Each substance was used in a base consisting of 1 part lanolin and 9 parts petrolatum and the base itself was

(1) Acta dermat ve erel 37 435 439 1957

used as a control Strong to complete inhibition of the eczematous reaction resulting from electrophoresis occurred in 3 instances with hydrocortisone 21 xanthogen ethanolamine and in 2 instances with fluorohydrocortisone Weak to moderate inhibition occurred in 10 experiments with the new substance 5 with hydrocortisone acetate 9 with fluorohydrocortisone and 1 with the control The results indicate that hydrocortisone 21 xanthogen ethanolamine is about as effective as fluorohydrocortisone when applied topically for the purpose of inhibiting experimental eczema

In clinical trials the new derivative was used in an ointment base made by mixing equal parts of two ointments (1) hydrocortisone xanthogenic acid in petrolatum and (2) ethanolamine in petrolatum 42 5% mono-olein 2 5% lanolin 5% and water 50% The effectiveness of this mixture containing 1% hydrocortisone 21 xanthogen ethanolamine was compared with that of a commercial ointment containing 1% hydrocortisone acetate in 81 cases of eczema and 38 of atopic dermatitis The new derivative was more effective in 42 instances hydrocortisone acetate was more effective in 12 instances and there was no difference in 66 The author concludes that the clinical effectiveness of the new preparation is somewhat greater than that of hydrocortisone acetate and is apparently about equal to that of fluorohydrocortisone It is much less apt to produce general effects when absorbed locally however since it is broken down to hydrocortisone which is much less active than fluorohydrocortisone The problem of stability of hydrocortisone 21 xanthogen ethanolamine has been solved by dispensing the preparation in a special double tube the xanthogen and ethanolamine components to be mixed before application

► (New corticosteroid compounds for topical application continue to become available We have no personal experience with the particular compound tested by *Haxthausen* Of the newer compounds which we have evaluated triamcinolone acetonide has been the most promising Paired comparison tests in many instances showed a 0 1% concentration of this substance to be somewhat *more effective* than 1% hydrocortisone 0 2% triamcinolone acetonide in turn appeared somewhat more effective than 0 1% in most cases Whether the topical effectiveness of this compound can be augmented by *increasing* its concentration remained unanswered as does the question What is the optimal concentration from the economic viewpoint

Perhaps the day is not far off when the pharmaceutical industry will develop corticosteroid compounds for topical application which will have

different therapeutic effects on different diseases of the skin It is entirely conceivable that one compound may prove more beneficial in the management of certain cutaneous lesions or processes while another compound may be found preferable for the treatment of others —Eds]

Clinical Trial P D C Kinmont[4] (*Derbyshire Royal Infirm Derby England*) discusses the planning conduct and expression of results of a comparative clinical trial of local applications on the skin It is essential to discuss the initial plan with the statisticians at an early stage to eliminate statistical objections The amount of detailed information which the trial is expected to produce should be limited If many observations are required it is difficult to cope with more than 4 preparations at a time The cardinal propertie for agents for external use as laid down by Sulzberger and Baer are useful in assessing a local application These are (1) high efficiency (2) low allergenic potential (3) very low local primary irritancy (4) low incidence of neoplastic change after long use (5) low systemic toxicity by absorption (6) ease of incorporation and stability in suitable vehicles and (7) acceptability to users

The author records the results of a controlled comparative clinical trial of a synthetic tar and of a prepared coal tar BP in a hydrocarbon base and in oil in water base The formula for the synthetic tar was phenol and o cresol 4 17% each quinoline pyridine and picoline 2 08% each toluene 8 33% xylene and anthracene 4 17% each phenanthracene 16 66% carbazole 10 43% and naphthalene 41 66% Of this mixture 0 24% was equivalent to 1% of prepared coal tar BP Both tar preparations were used clinically in concentration of 3% or equivalent

A total of 603 observations made on 281 patients was subjected to statistical analysis The synthetic tar proved more efficient less liable to produce adverse reactions and cosmetically superior to the prepared coal tar BP The synthetic tar was superior in eczemas of childhood adult atopic eczema and psoriasis There was little evidence that one base was superior to the other Both preparations were stable in suitable vehicles under ordinary ranges of temperature and under normal conditions of transport and storage The synthetic tar is of constant composition whereas the prepared coal tar is inherently variable

(4) A M A Arch Dermat 77 635 641 June 1958

► [The improved decolorized and synthetic coal tar preparations as well as coal tar extracts which we have had the opportunity to evaluate have never quite measured up to the therapeutic achievements of ordinary crude coal tar However under practical conditions nonmessy tar preparations and extracts often are preferable to crude coal tar One of the very important drawbacks to crude coal tar is the variation in chemical composition from one batch to another this can be reflected in the differences in the therapeutic effectiveness of the different batches

To the cardinal properties required for topical medicaments listed by the author one must add (8) lack of photodynamic and photoallergenic potential and (9) lack of immunochemical relationship to commonly encountered potent allergenic sensitizing agents —Eds]

Critical Evaluation of Effect of Steroid Lotions on Inflammatory Dermatoses Ira Leo Schamberg Samuel I Askovitz and Marvin Greenberg[5] (Albert Einstein Med Center) used the double blind paired comparison method in studying the effect of three steroid lotions and a control lotion in 510 patients with inflammatory dermatoses A newly devised statistical method was used that utilizes the large percentage of patients in whom there was no difference in effect and which weighs the degree of difference in response to the agents studied

In 177 patients in whom 0 1% fludrocortisone lotion was compared with control lotion base no statistically significant difference in effect could be demonstrated The lotion base was an oil in water emulsion containing Ceramol (a carbowax) diglycol stearate liquid petrolatum glycerin 6 5% isopropyl alcohol and 0 15% methylparaben The patients had the following diseases atopic dermatitis 25 patients contact dermatitis 38 eczematous dermatitis 5 generalized erythroderma and exfoliative dermatitis 2 eczematous hand eruptions 9 hyperhidrosis and hyperhidrotic dermatitis 1 infectious eczematous dermatitis 1 intertrigo and intertriginous moniliasis 11 lichen simplex chronicus 27 miliaria 8 generalized neurodermatitis 11 nummular eczema 10 psoriasis 2 seborrheic dermatitis 14 stasis dermatitis 4 and miscellaneous inflammatory dermatoses 9

Analysis by age sex diagnosis skin thickness and presence or absence of stratum corneum in areas of dermatitis revealed no group with significant benefit from the steroid lotion as compared with the control lotion In 217 patients no significant difference was found between the effect of 0 1% fludrocortisone lotion and 1% hydrocortisone lotion nor in

(5) A M A Arch Derm 78 490 499 Oct ber 1958

116 patients between the effect of 1% hydrocortisone lotion and 1% prednisolone lotion

The authors believe the following factors explain the discrepancy between the findings in this study and the experience of most dermatologists (1) It is probable that many of the patients were placebo reactors which explains in part not only the lack of significant superiority of the steroid over the base, but also the large percentage of patients (54 8%) in whom the two were equal (2) It is difficult to evaluate the effect of drugs on disease in which a large psychosomatic factor is present Most dermatologists agree that the psyche plays an important role in many inflammatory dermatoses (3) In the essentially unselected group of patients studied, the large number of dermatoses unaffected by steroids obscured the few benefited (4) The irritant effect of the alcoholic lotion may have overshadowed any beneficial steroid effect in many acute cases (5) Only 15 cc of lotion was available for treatment of each area The amount may have been insufficient to bring about improvement in some patients (6) Poor penetration of the steroid through thick intact skin may have prevented demonstrable benefit in some patients (7) Objective improvement may have occurred in the control area due to relief from pruritus thus obscuring the beneficial effect of the steroid The first three factors are probably the major ones The placebo reactor is an especially important potential source of error in studies on the effect of therapeutic agents

► [One of the difficulties in this study appears to be that a large number of the patients had eruptions which are not expected to be benefited by *topically applied corticosteroid preparations A factor possibly responsible* for bilateral improvement which was not considered by the authors is the effect of the corticosteroid preparations on distant sites (by way of external spread?) which often has been reported *In a planned study such as* this the patient should be carefully instructed to use different fingers when applying the two preparations to avoid contamination of the placebo treated areas with the corticosteroid *Despite these factors* and the other *described* by the authors we *have not had any difficulties in demonstrating* significant differences in the therapeutic effectiveness between corticosteroid and placebo preparations as well as between different corticosteroid medications This can be achieved by using not only the paired comparison method but by selecting patients in whom beneficial effect can be expected from the active medication —Eds]

Injection of Hydrocortisone into Dermatologic Lesions was carried out by *Leonard E Savitt*[8] *(Los Angeles)* In

(6) A M A Arch Dermat 76 780 8 December 195

most cases hydrocortisone sodium succinate (Solu Cortef) 50 mg/ml was injected locally in weekly doses of 25 50 mg/injection for 4-8 weeks Since pain was often produced when normal saline was used as the recommended diluent 2% procaine was substituted to lessen the pain For comparison in some patients a suspension of hydrocortisone acetate 50 mg/ml was used The intralesional injections apparently had no adverse effects Care was taken that the injection did not cause blanching When blanching was inadvertently induced it caused a minute slough that readily healed

Some improvement occurred in 31 of 39 patients Raised lesions responded better than relatively flat ones Localized lesions improved more readily than diffuse ones Firm lesions such as keloids responded poorly The indurated lesions of chronic discoid lupus erythematosus decreased in size whereas somewhat flat lesions did not Lesions of sarcoidosis that responded soon relapsed

Improvement of 75 100% occurred in 2 of 7 cases of discoid lupus erythematosus 1 of 2 cases of localized myxedema of the legs 1 of 2 cases of sarcoidosis 2 of 3 cases of lichen simplex chronicus (which had failed to respond to other modalities) 3 cases of cystic acne of the neck 2 of 3 cases of granuloma annulare 1 of 2 lesions of necrobiosis lipoidica diabeticorum in the same patient 6 cases of ganglions of the hands or wrists 1 synovial cyst on the index finger 1 case of hidradenitis suppurativa and 1 case of xanthoma tuberosum In a patient with chondrodermatitis nodularis chronica helicis pain disappeared after 1 injection and the lesion decreased in size 50% after 4 injections Three patients with keloids responded poorly but there was no recurrence in 1 case in which excision was followed by injection of hydrocortisone No improvement occurred in 2 cases of granuloma of the axillae caused by deodorant and 1 case of foreign body granuloma Improvement was about 50% with repeated injections in a case of vitiligo Pruritus in a case of lichen planus of the vulva was relieved

Hydrocortisone acetate is more useful than hydrocortisone sodium succinate for intralesional use because the latter causes more pain on injection and must be used within 24 hours after dilution

► [Intralesional injections of suspensions of hydrocortisone and other cor

ticosteroids deserve a trial in selected cases of alopecia areata lichen simplex chronicus hypertrophic lichen planus necrobiosis lipoidica (see following abstract) cystic acne and other circumscribed dermatoses Apparently the insoluble preparations generally do better than the soluble ones Atrophy of the skin is the most disagreeable side effect this atrophy varices considerably in degree and duration It is our impression that this can be minimized by not forcing the suspension into the skin too superficially —Eds]

Hydrocortisone in Necrobiosis Lipoidica Diabeticorum R H Marten and M Dulake (King s College Hosp London) treated 18 lesions of necrobiosis lipoidica diabeticorum in 4 patients with local injections of hydrocortisone Four lesions were treated with a solution containing 50 mg hydrocortisone acetate/ml normal saline containing 0 3% sodium carboxymethyl cellulose and 14 lesions were treated with a solution containing 25 mg /ml As controls 5 lesions were treated with the base solution only The volume of hydrocortisone solution injected depended on the size of the lesions and varied from 0 05 to 2 ml The amount often decreased as improvement occurred Injections were given at weekly intervals varied in number from 1 to 12 and averaged 4 6

Nine lesions treated with hydrocortisone injections disappeared completely or showed only residual discoloration In 8 lesions there was marked improvement, but slight elevation or induration persisted One lesion showed only slight improvement Injections containing 50 mg /ml were no more effective than those containing 25 mg /ml Three control lesions were unchanged and 2 showed slight improvement Histologic sections taken at various intervals during treatment with hydrocortisone showed all gradations between the fully active lesions and complete healing by fibrosis Partly healed lesions showed a decrease in the number of chronic inflammatory cells and disappearance of the degenerate areas of collagen

Response to treatment appeared to be independent of the age of the patient duration severity and control of diabetes and age of the lesions The site of the lesion did not appear to influence response to treatment except that lesions directly overlying bone were often more difficult to inoculate and were prone to ulceration Injections especially in the case of larger lesions were often difficult and painful at first

(7) Brit J Dermat 69 395 399 November 1957

but with continued treatment the lesions became softer and the solution spread easily and painlessly

Ulceration in which hydrocortisone injections were considered to have been a precipitating factor occurred on 3 occasions Two ulcers followed injections of the 50-mg solution and occurred within 24 hours of the first injection in 1 case and after 6 injections in the second case The third ulcer occurred a few hours after the first injection of the 25 mg solution When the ulcers healed they did so with apparently normal scar tissue A further complication was the development of cellulitis in 2 patients

► [The fact that ulcerat on of necrobiosis lipoidica lesions followed local injection with hydrocortisone is noteworthy In our experience to date when hydrocortisone has been injected into tissues underlying hypertrophic lichen planus (al) of the shin) alopecia areata (on the scalp) and chronic discoid lupus erythematosus over the malar region in no instances have we een ulceration Apparently le ions of necrobiosis are prone to ulcerate after injections of hydrocortisone —Eds]

Hair Regrowth in Alopecia Areata and Maligna Following Intracutaneous Injection of Hydrocortisone K W Kalkoff and E Macher[8] (Marburg Germany) injected about 50 mg hydrocortisone (in 2 cc) intracutaneously daily in up to 20 single wheals into the scalp of patients with alopecia maligna in whom hair growth had been absent for many



F g 1 – Spo ta ou (wh t) d p oked (p gmented) ha g wth d by d t m t l n P ocat d dm tra f hyd oc rt on al ((Court y f F lk ff h W d M h E H tarzt 9 441-451 O er 1958)

(8) H t 9 441 451 O tobe 19 8

years Injections were given at the border of the cutis and subcutis and not too deeply Similar treatment was given to patients with alopecia areata Results were checked clinically and histologically

In the patches of alopecia areata and maligna regular growth of pigmented hair of normal thickness limited to the areas of injection was observed 3 5 weeks after the injections (Fig 1) The lymphocytic infiltrations characteristically found around the papilla and the hair bulb disappeared under the influence of hydrocortisone and pigment formation began again in the matrix Intracutaneous injections of hydrocortisone did not stimulate any hair growth in alopecia atrophicans or in alopecia prematura

The practical value of the hydrocortisone effect is limited since in the non self limited cases of alopecia areata the patient loses his hair again after the effect has subsided

► [The dermatologist has the advantage of having available the systemic topical and intracutaneous routes of administration for hydrocortisone and its analogues each with its own indications for the management of certain diseases of the skin —Eds]

Vibrapuncture Technic in Treatment of Localized Neurodermatitis Preliminary Study on Effect of Hydrocortisone Acetate Injected by Multiple Vibrapuncture Method into Areas of Lichen Simplex Chronicus is presented by Joseph N Aaron Irwin Kantor and Harold Stromeyer[9] (Mount Sinai Hosp New York) Five patients with lichen simplex chronicus of long duration were treated The Conway Dermajector was used with needles set for 2 3 mm length The most effective oscillation rate of the needles was 3 000 3 500 rpm A *suspension of hydrocortisone acetate containing 25 mg /cc* was used All patients tolerated the procedure without anesthesia All had relief from pruritus within 24 hours and clinical improvement in the appearance of the lesions resulted in each case The number of times each area was treated depended on the degree of lichenification No residual atrophy was noted during or after treatment All patients who were treated had proved resistant to other forms of therapy

► [Apparently the principal advantage of this mode of administration of hydrocortisone suspension over intracutaneous injection is that it does not produce atrophy The question arises whether the absence of atrophy following treatment of lichen simplex chronicus by this method assures

(9) A M A Arch Dermat 77 576 580 May 1958

the therapist that no atrophy will occur after treatment of other dermatoses by the same technic —Eds]

Cadmium Sulfide Suspension in Seborrhea Capitis William L Kirby[1] (Bowman Gray School of Medicine) describe a method of treating 84 patients with seborrhea capitis

METHOD —Patients were asked to wet the hair rub in a 2% suspension of cadmium sulfide shampoo for 2 3 minutes rinse the hair thoroughly massage a second application into the scalp for not less than 5 minutes and again rinse the scalp Shampooing twice weekly was advised in the more severe cases and once weekly in the milder ones

Of 80 patients adequately followed 79 reported good to excellent results Six with seborrhea oleosa responded satisfactorily although 2 had used selenium disulfide shampoo without benefit The scalp condition of 8 with seborrheic dermatitis was satisfactorily controlled in 4-6 weeks Of 51 with seborrhea sicca 50 had good to excellent results One had shampoos twice weekly for 4 weeks without improvement Fifteen had seborrhea steatoides in some the condition was severe but response was excellent in all None required more than 12 treatments

Most patients with milder forms of seborrhea were able to decrease the frequency of shampoos after 3 or 4 weeks to every 2 weeks and after 8-10 weeks to every 3 or 4 weeks There were no complaints of excessive oiliness or dryness after using cadmium sulfide shampoo No instances of primary irritation or sensitivity reactions were encountered

► [New antiseborrheic agents some marketed as ethical drugs and others as proprietaries have become available with such frequency that it is difficult to remember all their names It is also unusual that one can turn on a television set without being exposed to the view of a gorgeous blonde who is waving her Lorelei like hair back and forth to demonstrate the superb effect of a new dandruff remover

While we have had satisfactory results with the cadmium sulfide shampoo as used by Kirby they do not approach the figure of almost 100% Occasionally it causes oiliness though nowhere nearly as often as selenium sulfide suspension in several of our cases it has caused excessively oily hair —Eds]

Treatment of Warts with Cantharidin is described by William L Epstein and Albert M Kligman[2] (Univ of Pennsylvania)

METHOD —A drop of solution containing 0 7% cantharidin in equal parts of acetone and flexible collodion is rubbed over the wart the application being confined to the wart itself Paring or other prior

(1) J I t Derm t 29 159 160 S pt mbe 1957
(2) A M A A h De mat 77 508 511 M y 1958

treatment is unnecessary. After the solution dries a small piece of plastic adhesive tape slightly larger than the wart is applied. The preparation is kept in place by covering it with a Band-Aid[8] or gauze dressing. It is recommended that the dressing be kept in place until the patient's return in 7-10 days. It may, however, be removed after 48 hours or less if there is marked pain or tenderness.

Ordinarily a frank blister forms within 24 hours, but personal responses vary. The obviously altered, dead or blistered skin is debrided with knife or scissors on the next visit. One application is often enough, but reapplication should be made at weekly intervals as long as wart tissue persists.

The authors treated 113 warts in 61 patients. Immediate clinical cure lasting at least 3-6 weeks occurred in 66 of 69 ordinary warts, 20 of 27 plantar warts, 11 of 12 periungual and subungual warts and 2 of 5 mosaic warts. Many patients required only 1 treatment and most responded to fewer than 3 applications. Severe painful reactions occurred in 4 patients. Recurrences were noted in 6 of 42 plain warts and 4 of 14 plantar warts followed for 6 months.

Cantharidin is no more effective than other destructive technics, perhaps less so than electrosurgery. Its virtue lies in its simplicity and lack of residual scarring. It is especially useful in the treatment of warts in children.

► [Another worthwhile addition to the therapeutic armamentarium for these exceedingly common lesions.—Eds.]

Local Therapy of Oral Leukoplakia with Vitamin A. Dattatreya N. Mulay and Frederick Urbach[3] (Roswell Park Mem'l Inst., Buffalo) treated 10 patients with typical oral leukoplakia of 3 months' to 10 years' duration with oral troches containing 150,000 units of vitamin A each. Severity of the leukoplakia ranged from grades II to IV (Thoma). The patients were instructed to remove their dentures and allow 1 troche to dissolve slowly in the mouth 2-3 times daily. Treatment periods varied from 2 to 6 months. Seven of the patients showed pronounced improvement, with 70% clearing or better; 1, slight improvement; 2 (1 of whom took the troches only *intermittently*), *no improvement*.

It is known that a number of medicinally active compounds (cortisone, desoxycorticosterone, etc.) are absorbed easily through the mucosa, even though they penetrate the intact skin poorly. The present results indicate that vitamin A penetrates plaques of oral leukoplakia when applied topically

(3) A.M.A. Arch. Dermat. [illegible]8:637-639, November, 1958.

The beneficial effect probably is connected with interference with pathologic keratinization Duration of the beneficial effect was not determined

► [It is difficult to assess the efficacy of topical treatment in oral leukoplakia unless the condition is very pronounced and disappears completely under treatment and unless similar troches not containing vitamin A have been used in control cases —Ed]

Chloranil in Treatment of Psoriasis Substitute for Chrysarobin Walter O Teichmann and Peter N Horvath[4] (Washington D C) treated 93 patients with psoriasis with 5 or 10% chloranil (tetrachloro p benzoquinone) in a polyethylene glycol base Patients were instructed to apply the ointment thinly at bedtime and to rub it in thoroughly so no excess remained Chloranil stains the skin a light brown which usually is not troublesome if desired it may be removed with a fat solvent such as petroleum benzin

Considerable improvement was observed in 55 patients moderate improvement in 24 and no improvement in 10 The process of resolution is similar to that of chrysarobin or coal tar therapy The lesions first lose their scales become less elevated and in the most responsive cases finally break up into small areas and fade away The most marked improvement was observed during the first month of treatment In several patients the lesions retrogressed when treatment was stopped and improved again on reapplication of the drug No posttreatment leukoderma was noted Chloranil was most effective against the typical psoriatic plaque characterized by heavy scales It appeared to benefit palmar and plantar plaques and intertriginous lesions but was least effective against small guttate lesions Control areas treated with ointment base showed no improvement in 10 of 24 patients slight improvement (not equivalent to that of areas treated with chloranil) in 12 and improvement equal to that of areas treated with chloranil in 2 patients

One instance of true sensitization to chloranil was observed In 5 other patients primary irritation resulted from use of 10% ointment but not with 5%

► [We have tried this compound in a weaker concentration and only in seborrheic dermatitis and psoriasis of the scalp In some of the cases it seemed to be quite effective —Eds]

New Approach to Control of Acne Vulgaris Because at

(4) S M J 50 15 1 1523 Dec mbe 1957

times acne vulgaris is more severe in tropical climates whe sweating is increased Thelma Golub Warshaw[5] (New Yo Infirm) assayed the clinical effect of decreased sweating patients with this disease After each face wash, 33 patien applied 20% aqueous solution of aluminum hydroxychlori to the entire face, except the periorbital area Treatme was continued for 3 weeks to 6 months All patients also us topical preparations containing resorcin and sulfur and we given routine instructions on the care of acne vulgaris control group of 33 patients received similar treatment e cept that aluminum hydroxychloride was not used

Clinical improvement with a decrease of comedones oil ness and pustules was observed in 32 of the 33 patients treate with aluminum hydroxychloride The aluminum preparatio seemed to accelerate initial clearing and easily maintaine the skin in a less oily acne free condition The only sid effect reported was the deposit of a saltlike substance on th skin that could be removed easily by washing Improvemen was less rapid and less well maintained in the control grou

The rate of fat (sebum) spreading over a wet skin is of th order of at least 10^3 times the rate of flow and spread on dry skin Also, variations in the level of ether soluble sub stances (fats) on skin directly parallel the level of sweat de livery in the skin area Thus the use of an aluminum salt a an antiperspirant and consequently as an empiric sebaceou gland inhibitor seems logical

► [In our experience aluminum hydroxychloride solution or similar prep arations sometimes aid in decreasing the oiliness of the face in patients with or without acne vulgaris —Eds]

Primary Irritant Activity of Barrier Creams J Tas[6] (Ha dassah Univ Hosp Jerusalem) performed 48 hour patch tests with 6 different barrier creams on 300 patients most of whom had eczema Oil resistant creams caused a high per centage of positive reactions Kerodex* B D gave 49 7 and Magnor red 25% positive reaction The water resistant creams Magnor white (14 7% positive) and Kerodex* B W (3 7%) showed a much lower incidence of positive reaction The percentage of positive reactions with silicone creams wa still lower positive reactions with Covicone* occurred in 2% and with Silicote in 0 7% of cases

(5) New York J Med 7 3999 4000 Dec 15 195
(6) J Invest Dermat 9 3 25 September 1

Most reactions were of the primary irritant type characterized by circumscribed erythema or by a blister but in 5 instances eczematous reactions were observed The high incidence of positive reactions to some of the creams does not detract from their considerable prophylactic usefulness Actual use of the barrier creams in which they are applied for a few hours without covering is different from application for 48 hours under an occlusive bandage as in patch tests The well known clinical fact that barrier creams easily provoke exacerbation in inflamed skin can be explained by the slightly irritant action of the creams Therefore they should be used only on healthy skin for prophylactic purposes

► [The high degree of primary irritancy of some of these creams itself presumably severely limits their use There is very little discussion now of barrier creams as compared with a few years ago We suspect that this is due to th generally poor results with these protective creams —Eds]

Experimental and Clinical Studies on Mode of Action of Atabrine and Chloroquine in Chronic Lupus Erythematosus were conducted by A Wiskemann and H Koch[7] (Univ Skin Clinic Hamburg Eppendorf Germany) When compared with commonly used commercially available light protective ointments 10% atabrine and chloroquine emulsions 10% showed effective light protection from erythema producing ultraviolet light of medium wave length About 30% of the light protective action is probably not absorptive but biologically determined When the ointments were applied immediately after exposure to ultraviolet light no biologic light protective effect could be demonstrated

Butazolidin® administered intramuscularly increased the ultraviolet erythema threshold only when it was given before the irradiation

The biologic light protective effect probably consists of a nonspecific antiphlogistic action After 3 days of administration atabrine and chloroquine showed a definite antiphlogistic effect in the rat paw test The dose used corresponded to 5 times the maximum daily human dose The antiphlogistic effect was less pronounced than that of cortisone The superiority of atabrine and chloroquine over cortisone in the treatment of chronic lupus erythematosus is probably due to differing modes of action and different distribution in various organs

( ) H ta t 9 215 218 M y 1958

In 22 patients with chronic lupus erythematosus who did not receive any chloroquine by mouth for at least 4 weeks 8 weeks of therapy with chloroquine ointments was ineffective Since the light protective effect of the ointments must be superior to the protection offered by oral administration of the same drugs it can be assumed that the absorptive light protective effect of chloroquine does not play an important role in the treatment of this condition The antiphlogistic action of the ointments was not effective either

In experimentally photosensitized or pathologically photosensitive skins chloroquine ointment also gave protection against ultraviolet light of long waves This was considerable when the maximum absorption capacity of chloroquine at *320 340* mμ and the wavelength of the causative light corresponded with each other

So called Decubitus Ulcer Pathogenesis Prophylaxis and Treatment are discussed by L Justin Besançon H Péquignot, J -P Etienne, J Savier and R Vilain [8] Pressure on points of contact aggravated by loss of sensitivity and mobility and by impairment of muscular tone gradually or suddenly produces a true infarct of the soft tissues which leads to ulceration The course of the ulcer evolves in three stages elimination of necrotic material filling and marginal epidermization

Prophylaxis of this complication demands a judicious evaluation of the risk by the physician correct interpretation by the nurse of the lesion at onset when still reversible and use of preventive methods especially massage On admission patients should be divided into major and minor risks The former are placed immediately on the alternating mattress and are given massage twice daily Inspection of buttocks and heels requires turning once or twice daily and placing a groove for the heels Major risk patients include all those who are completely immobile with loss of activity i e those with comas of all types hemiplegia paraplegia cachexia with decreased movement and serious heart failure In minor risk patients a single daily massage is sufficient but pressure points should be inspected each day and if the cutaneous condition is not being controlled prophylaxis is stepped up with 2 massages a day on the special mattress

(8) Semaine hop Paris 33 4115 4121 Dec 10 57

Once decubitus has developed general treatment should consist of control of anemia and malnutrition by small transfusion of blood and deplasmatized erythrocytes Tube feeding often is inadequate and every effort should be made to reestablish normal feeding by mouth Local treatment has two objectives to correct the atrophy and to cleanse the lesion Massage should not be discontinued because it favors vascularization of the defect accelerate elimination of devitalized tissue and prevents trochanteric or ischiatic lesions If the patient cannot move spontaneously in lateral decubitus the alternating mattress permit still vital tissues on the periphery of the ulcer to maintain trophicity On the denuded plaque a daily lavage with soap or detergent combined with a rub with alcohol is an excellent prelude to massage A dressing is unnecessary For dry ulceration a dressing is also useless excision is the only effective measure but this is usually impossible since the underlying disease is at its height When general state improves and the ulcer commences to become detached the black plaque may be excised and the resection should be sufficiently extensive to remove all necrotic tissue A dry dressing should be applied A sheet of cellophane separates the body dressing and protects the cloth from oozing A body bandage is preferable to adhesive which often causes erythema To aid in surgical drainage Dakin s solution and trypsin powder are used

When the wound is completely freshened cicatrization is inevitable but it is sometimes retarded by permanent dorsal decubitus position (paraplegics) malnutrition encroachment of skin at the edges of the lesion which may delay the regeneration of marginal epidermis and an ulcerated callus which resists spontaneous scarring

► [The American version of the alternating mattress is made of plastic and consists of a series of tubular longitudinal spaces which alternately are filled with air and then collapsed This is done by means of an automatic pump To produce a massaging action every other tube is filled while the in between ones are left collapsed At appropriate time intervals the collapsed tubes are filled and the filled ones are allowed to collapse thus producing a continuous and regular massaging action.

Proteolytic enzymes other than trypsin are available in this country and are used to debride necrotic ulcers —Eds]

Preventive Measures against Skin Injuries from Cold Wave Developers are outlined by Siegfried Borelli[9] (Univ

(9) [illegible] 8 40 546 December 1957

of Munich) Compounds used in making cold waves (permanent) affect the skin in two ways they cause swelling and loosening of the corneal layer and exert a nonspecific alkali effect Hyperhidrosis may also develop The simultaneous use of thioglycol and alkali increases these effects and preventive measures must be directed against them To prevent both, but especially the keratolytic effect hairdressers have been advised to treat with H_2O_2 and an acid rinsing solution after each application not only the customer's hair but their own hands The aim is to neutralize the effect of thioglycol Unfortunately most hairdressers have not followed these suggestions and even refused them with the excuse that the fixing solutions irritated their skin

More than 200 hairdressers engaged routinely in preparing cold waves were studied concerning the best method to protect the skin of their hands Use of the usual fixation solutions alone did not give any protection and often even aggravated the skin changes Application of fatty ointments seemed to be the most effective Various ointments gave practically the same benefit as long as they contained some fat The best protection was achieved when the hairdresser applied some fatty ointment to his hands before each cold wave application and rinsed his hands with the fixing solutions afterward followed again by a fatty ointment The simultaneous application 2 or 3 times daily of an astringent such as Taktokut (symm dichlorphenylsulfonyl polyamino benzolsulfonyl di aminophenylsulfonacetic ammonium) which is a synthetic tanning agent will effectively suppress hyperhidrosis

B Systemic Drug Therapy

Experimental Ringworm in Guinea Pigs Oral Treatment with Griseofulvin is described by J C Gentles[1] (Univ of Glasgow) Griseofulvin a metabolic product of several penicillium species is markedly fungistatic to many fungi in vitro, and in plants it shows systemic antifungou activity It is reported to have low mammalian toxicity

Guinea pigs were infected with *Microsporum canis* and treatment with griseofulvin was started 10 days later when

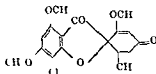
(1) Nature London 182 476-47 Aug 16 1958

lesions were well developed Daily dosage was 60 mg/kg control animals were given unmedicated tablets Clinical improvement was noted within 4 days and the highly inflammatory reaction which occurred in all control animals was prevented in the treated guinea pigs Among the latter group about half the hair follicles were shown histologically to be infected after 4 treatments By the 8th treatment few infected follicles could be found Skin sections of the untreated animals showed heavy infection of almost all hair follicles at this time Under Wood light infected hairs of treated animals fluoresced only at the tips and microscopic examination revealed the dermatophyte only in the upper part of the hair shaft Apparently the uninfected part of the hair formed during treatment was resistant to invasion by the fungus

Similar experiments have indicated that griseofulvin is equally effective when given orally to guinea pigs infected with Trichophyton mentagrophytes It has also been used successfully in treatment of T verrucosum ringworm induced in cattle In vitro it is active in low concentrations against all the common dermatophytes

► [This report while dealing with the effects of griseofulvin in fungous infected laboratory animals is likely to turn out to be one of historic importance in dermatology If these results in laboratory animals and the preliminary favorable results thus far obtained in man are not marred by as yet undiscovered prohibitive side effects we may be on the threshold of the era of truly specific systemic control of superficial fungous infections

The chemical structure of griseofulvin has been reported to be



Apparently the drug has fungistatic rather than fungicidal properties and its unique therapeutic efficacy is based on its selective capacity to combine with keratin Since its chemical constitution is known there is no reason why the chemists should not be able to provide us with related compounds with different and perhaps better therapeutic efficacy

Among the innumerable questions which will have to be answered are Can fungous infections truly be eradicated by a single course of griseofulvin or will repeated courses of treatment be necessary as is often the case in the management of furunculosis with broad spectrum antibiotics? If single courses are effective how long will the drug have to be given? Will some strains of fungi develop resistance?

Apart from its promise as a specific therapeutic agent for some of the most common dermatoses griseofulvin may turn out to be a wonderful

tool for the scientific investigation of the mechanism underlying resistance and susceptibility to superficial fungous infections. Further it may help in solving some of the more puzzling clinical syndromes connected with fungous diseases such as which eruptions are or are not id. Perhaps some dermatologic entities hitherto suspected or unsuspected of having a fungous etiology will be shown definitely to be caused by a fungous infection.

Dr Harvey Blank of the University of Miami reported at the December 1958 meeting of the American Academy of Dermatology and Syphilology on the therapeutic effectiveness of griseofulvin administered systemically in the management of certain superficial fungous infections of the skin. Although the number of patients treated was limited and the follow up period short, this antibiotic promises to be a distinct contribution to dermatologic therapy.—Eds.]

Disseminated Coccidioidomycosis Treated with Amphotericin B Amphotericin B is an antibiotic derived from a species of streptomyces found in a soil sample from Venezuela. In vitro it has antifungous properties for a wide variety of organisms including *Coccidioides immitis*. In vivo it has an ameliorating effect on mice experimentally infected with *C immitis*.

Robert C Hunter Jr and Edward S Mongan (William Beaumont Army Hosp) treated 4 patients with disseminated coccidioidomycosis with amphotericin B. One received about 5 Gm daily by mouth for 38 days. He was already recovering when the drug was started and there was no reason to believe it altered the course of the disease. Three were given amphotericin B intravenously for 3-12 months, and all 3 reacted predictably with anorexia, nausea, chills and fever after every infusion. Severity of the reactions tended to decrease slightly with continued medication. Salicylates and antihistamines did not alter the reactions. All 3 patients had elevated blood urea nitrogen one or more times during treatment, which subsided on interrupting treatment for 1-2 weeks. Because of the side reactions, the dose was limited to 50 mg in 5% dextrose solution, which was given slowly over 6 hours every other day after supper.

Results of treatment in a disease as unpredictable as disseminated coccidioidomycosis must be accepted with caution. All 3 patients improved while on intravenous amphotericin B therapy, but response was slow. After months of treatment C immitis could be cultured from a variety of areas in these patients. In 2 of the patients 20-25 mg amphotericin B was injected directly into 7 coccidioidal abscesses 1-3 times about

(2) U S Armed Forces M J 9 14-4 1486 Oct ber 1958

1 week apart Response was uniformly favorable and fluctuation disappeared in 3-6 weeks

Results with amphotericin B intravenously indicate that it possibly was useful in treating di emminated coccidioidomycosis Results with direct injection of ab cesse were more impressive Amphotericin B probably repre ents the first real advance in treatment of disseminated coccidioidomycosis but further clinical testing is essential

► [With griseofulvin amphotericin B and Mycostatin® it certainly looks as if the pecific systemic or local antibiotic treatment of superficial and deep mycoses soon will be as much of a routine as the sy temic and local treatment of most bacterial diseases Unfortunately no similar progress has been made in the specific antibiotic treatment of virus di eases Successful intralesional injection therapy with amphotericin B in chromoblastomycosis of the skin and subcutaneous tissues has been reported by Co tello DeFeo and Harber —Eds]

Effect of Oral Steroid on Noninflammatory Scalp Ringworm Preliminary Report In a case of scalp ringworm in a boy aged 8 Naomi M Kanof[3] (Children s Ho p Washington D C) observed complete clearing in 6 weeks with oral systemic steroid therapy (5 mg prednisone 4 times daily) In 8 subsequent patients with noninflammatory tinea capitis due to Microsporum canis no complete cure has yet been achieved After 4 10 weeks therapy however all patients demonstrated markedly fewer broken-off fluorescent hairs or a change of the fluorescence from brilliant emerald green to grayish white All patients had been refractory to topical therapy and had involvement of at least two thirds of the scalp before steroid therapy was initiated

Further observations will be necessary to determine whether improvement will continue and permanent cure can be achieved It is not known whether the marked decrease in the number of fluorescent hairs and the change in the hue of fluorescence are evidence of an alteration in the infection proper or only a change in the phenomenon of fluorescence or whether the hair growth has been altered in such a manner as to retard or reject fungus invasion

► [Irrespecti e of whether *oral* steroids will eventually prove to be therapeutically effective and desirable in scalp ringworm these findings are of the greatest theoretical *interest* What is the mechanism which brings about the e strik ng changes Is it as Naomi Kanof suspects an effect on the hair cycle? Is it an effect on the fungi via a direct or indirect pharmacologic act on of the steroid compound or is it some *other effect*? —Eds]

(3) J I t Dermat 31 139 S p mb 19 8

Effects of Triamcinolone (Aristocort®) and 6 Methyl prednisolone (Medrol®) on Some Skin Diseases Therapeutic Note is presented by F Kalz[4] (Montreal) Triamcinolone was used in the treatment of 48 patients including 24 with severe atopic dermatitis 16 with other eczematous eruptions, 6 with psoriasis 1 with pemphigus and 1 with alopecia areata Treatment was started with 20 mg daily for 2 5 days and the dose was then reduced by 4 mg every 2 3 days until the minimal effective dose was found Response was satisfactory in all patients except 4 of the 6 with psoriasis In 21 of the 24 patients with atopic dermatitis a satisfactory maintenance dose averaging 6 mg daily could be established Three of these patients had side effects

Untoward side effects occurred in 8 patients in the entire group Epigastric pain occurred in 4 1 of whom showed reactivation of a duodenal ulcer Four patients had headaches and dizziness Minor side effects consisted of hyperhidrosis in 2 patients and acne in 1

Six patients who showed side effects with triamcinolone were given 6 methylprednisolone and all tolerated the drug well A number of other patients were treated with 6 methyl prednisolone alone At least one third higher dosage was required to obtain the same effect as with triamcinolone In 2 patients 6 methylprednisolone caused dizziness and tiredness These patients were able to take dexamethasone without side effects

Triamcinolone offers several advantages over prednisolone It does not cause sodium retention it rapidly controls the inflammatory phase of skin diseases and the effective maintenance dose is low Its disadvantage is a high incidence of minor side effects Though 6 methylprednisolone is less potent it is less apt to cause side effects

► [Both triamcinolone and methylprednisolone are valuable additions to the corticosteroid armamentarium among their principal advantages is the absence of sodium and water retaining properties Apparently cortisone and all its analogues so far used therapeutically have the capacity to produce weakness and muscular dystrophy provided the dose is large enough and the period of administration prolonged However with triamcinolone this side effect is encountered more often When muscle weakness develops with the use of any of the corticosteroids or ACTH they may have to be withdrawn before recovery of muscle strength is observed

Dexamethasone although effective in much smaller dose than the other

(4) Canad M A J 9 400 401 Sept 1 19 8

corticosteroid produces side effects at these lower dosages similar to the others produced at the high dosage level—Eds]

Use of Triamcinolone (Aristocort®) in Selected Dermatoses Results in 13 patients are described by Ben Kance[5] (Vancouver) Of 2 patients with systemic lupus erythematosus 1 did well initially with prednisone but required 30 mg daily for maintenance This dose resulted in moonface and some acne On changing to triamcinolone there was no improvement in the facies on a required daily dose of 24 mg Hirsutism dilated venules telangiectasia on the lower extremities and tiredness occurred on this dose On changing to methylprednisolone the daily requirement was reduced to 18 mg and the patient felt better subjectively although features similar to Cushing syndrome were retained The second patient originally maintained on cortisone showed considerable improvement with prednisone and now is showing still greater improvement with a maintenance dose of 14 mg triamcinolone

A patient with generalized scleroderma has been on a maintenance dose of 8 mg triamcinolone for 7 months as compared with 15 mg prednisone previously She has shown comparable clinical and subjective improvement though she is gradually losing weight and has bouts of anorexia and diarrhea which may be due to the drug or to intermittent influenza

Two patients with dermatitis herpetiformis failed to respond to triamcinolone in doses of 16-32 mg daily Triamcinolone 16 mg daily appeared to exert a favorable influence in the experimental treatment of 2 patients with alopecia areata Six patients with extensive and pruritic psoriasis showed a marked clinical and subjective response while being maintained on doses of 8 12 mg daily

Triamcinolone was stopped in only 1 instance because of side effects (symptoms of gastric ulcer with negative radiograph) Otherwise side effects were minor including features of Cushing s syndrome—moonface hirsutism acne telangiectasia dizziness flushing lack of energy tiredness and loss of appetite

► [From the dermatologic viewpoint perhaps the most important feature of triamcinolone is that it unquestionably appears to be in general more efficacious in psoriasis than the older and other newer steroids—Eds]

(5) Ca d M A J 79 748 751 N 1 1958

Triamcinolone in Treatment of Systemic Lupus Erythematosus Edmund L Dubois[6] (Univ of Southern California) treated 29 patients for up to 11 months Triamcinolone, an unsaturated prednisolone derivative is 1 3 times as powerful as prednisone and 4 4 times as potent as hydrocortisone as an anti inflammatory agent The amount of triamcinolone required by individual patients varied widely depending on the severity of the disease and sensitivity of the patient to the agent The average initial dose in a patient with a mild case of systemic lupus erythematosus was 20 6 mg daily The average maintenance dose used to control mild exacerbations was 26 mg daily There was no evidence of sodium retention or potassium loss Routine sodium restriction potassium supplementation and prophylactic ulcer diet were not used

Repeated gastrointestinal x ray studies in 16 patients revealed evidence of peptic ulceration in only 1 who received 96 mg daily No changes were observed in 9 who had gastric analyses with histamine every 2 months or in 13 who had 24 hour uropepsin determinations

The pattern of clinical improvement closely paralleled that obtained by previous treatment with older steroids All clinical and laboratory abnormalities except long standing renal involvement disappeared A major difference between triamcinolone and other steroids was a tendency in 18 patients toward progressive gradual weight loss averaging 7 8% of initial body weight

Cutaneous side effects particularly cushingoid appearance hirsutism and striae were more marked in women taking triamcinolone than with older steroids The most serious side effect was muscle weakness which appeared in 6 patients after 4 32 weeks of therapy There seemed to be no relation between dosage and this symptom The profound muscle weakness most marked in the quadriceps groups gradually cleared after several weeks of therapy with another steroid Male patients did not show these side effects Of 14 patients who had received prior steroid therapy with all the older anti inflammatory hormones 7 felt better and their disease was better controlled with triamcinolone

Treatment of Psoriasis and Other Dermatoses with Triamcinolone (Aristocort*) Walter B Shelley Joseph S

(6) J A M A 167 1590 1599 July 26 1958

Harun and Donald M Pillsbury[6] (Univ of Pennsylvania) treated 60 patients who had all forms types and degrees of psoriasis with triamcinolone a corticosteroid in doses of 12 16 mg daily by mouth In 36 response was prompt and unquestionable within a week the scaling and erythema di minished significantly and within 2-4 weeks of continued adequate dosage the psoriasi in some was completely erased This group presented the distinctive finding of local invo lution of psoriasis at the site of injection of triamcinolone in tradermally Relapses invariably occurred when the drug was withheld In view of the rapid relapse that invariably fol lowed suspension of therapy reduction of the dose to zero will probably offer great difficulty in many patients Topical use was without effect

A wide variety of reversible side effects was observed Some were favorable such as stimulation of hair growth in alopecia areata but many were unfavorable such as flushing hyperhidrosis facial hirsutism and facial contour changes Triamcinolone proved remarkably effective in treatment of alopecia areata This compound seems to have a specific stimulant effect on hair growth

Triamcinolone was highly antiallergic antirheumatic and anti inflammatory and therefore useful in various dermati tides Its use in psoriasis should probably be limited to acute extending cases that are not controllable by other means or to extensive severe chronic forms In common with all other antipsoriasis remedies this drug is no cure for psoriasis It must be recognized as purely palliative Triamcinolone is a strong corticosteroid with influences throughout the entire body It is not to be given for relief from a few scales on the elbows

Combination of Chloroquine and Prednisone in Treatment of Lupus Erythematosus was tried by A Midana and M Depaoli (Turin Italy) in 18 patients having chronic and subacute cases with localized and disseminated lesions The daily dose of chloroquine was 500-600 mg for 8 10 days then 250 mg for 4-8 weeks 15 mg prednisone was given daily for 10 days and 10 mg daily for 4 8 weeks

Comparison of results with those obtained with chloro

(6) J A.M A. 167 959 964 J 21 1958
(7) D rm t log 115 677 680 D ember 1957

quine alone showed that with the combined treatment there was more rapid fading of the lesions and absorption of the *edematous infiltrative process* which in some cases was striking These results were observed not only in circum scribed local lesions but also in 2 of 3 patients with dissem inated distribution in the extremities With addition of pred nisone chloroquine was better tolerated and complete courses of the drug could be given without troublesome side effects These results support the conclusions of others who have used cortical hormones combined with prolonged anti biotic and chemotherapeutic administration with good effect

Two possible explanations of the potentiating effect of small doses of cortical hormone are suggested (1) The pro found effect of prednisone on the function metabolism and proliferation of cells may lead to an increased concentra tion of chloroquine in the plasma owing to its retarded elim ination (2) Slowing of the progressive encapsulation of foci by the hormone may lead to a greater concentration of chlo roquine in these areas with more rapid regression of clinical manifestations

► [In subacute or acute disseminated lupus erythematosus as in other diseases it makes good sense to use in combination two therapeutic agents each of which by itself is capable of benefiting the disease With two such effective systemic medications given simultaneously it is usually po sible to reduce the required dose of both drugs thus lessening the chances for possible undesirable effects produced by each alone At times of course greater beneficial effects can be achieved with such combined treatment than with either drug alone —Eds]

Sclerema Neonatorum Report of Three Cases Treated with Cortisone is presented by P C Bajpai P Singh and U Bhatia[8] (Lucknow Med College)

CASE 1 —Boy aged 15 days had dyspnea feeble pulse diarrhea and rapid shallow respiration The skin over the body except for the palms soles and scrotum was thickened and indurated without pitting Treatment included oxygen subcutaneous and oral electrolyte solu tion Chlorostrep® for diarrhea and cortisone 5 mg daily for 2 days then 10 mg daily for 5 days Improvement was evident in the skin and general condition after 48 hour By the 8th day the skin was entirely normal *Recovery was complete in 10 day*

CASE 2 —Boy aged 10 days was critically ill with feeble rapid pulse rapid shallow respiration diarrhea subnormal temperature and generalized waxy pale thickened skin Cortisone was adminis tered in doses of 5 mg 3 times a day *for 3 days 10 mg* twice a day *for* 4 days and was then tapered off Improvement in the skin was no

(8) Indian J Pediat 4 207 212 July 1957

ticeable on the 3d day and the child seemed well except for diarrhea by the 6th day Symptoms of septicemia developed on the 10th day however and the child died the next day

CASE 3.—Boy aged 3 months had had diarrhea for 12 days The skin on the legs forearm and lower abdomen was stiffened and slightly thickened Dehydration and subnormal temperature were present Induration of the skin became more extensive despite treatment with fluid and sulfaguanidine but began to subside 3 days after cortisone and penicillin were started The child was well 6 days later

The authors feel that cortisone was primarily responsible for the improvement observed in these 3 patients During the past year 10 infants were treated without cortisone in Children s Hospital and Queen Mary s Hospital in Lucknow In each the sclerema neonatorum was fatal

► [Another report attesting to the often lifesaving and therefore "curative" effect of corticosteroids in this disease.—Eds]

Pemphigus Vulgaris under Prolonged Massive Treatment with ACTH and Cortisone I Urinary 17 Ketosteroid and 17 Hydroxycorticoid Excretion As some authors have described low values of 17 ketosteroid excretion as characteristic of pemphigus A Dostrovsky and F G Sulman[9] (Jerusalem) studied this problem before starting treatment in 21 cases of pemphigus Though within normal range the titer of 17 ketosteroid excretion in the urine of these patients tended toward low values and there was an unusual fluctuation of 8 28 mg /day not found in normal persons or in those with other diseases There was no noteworthy difference in 17 ketosteroid values during the period before treatment due to sex duration of disease or severity of attack There was no parallel between the titer of urinary 17 ketosteroid excretion and the result of the Thorn test

In 12 patients with generalized pemphigus vulgaris the 17 ketosteroid excretion was further studied under massive treatment with cortisone and ACTH during exacerbation and quiescence Treatment routines used were ACTH alone cortisone alone or alternating with ACTH and combined ACTH and cortisone

ACTH stimulated 17 ketosteroid excretion in all cases of active pemphigus particularly in the first attack and also in most relapses One case was refractory Cortisone inhibited 17 ketosteroid excretion The effect though not constant was evident even with small dose both in active stages and

(9) D m t l mea 116 65 90 F bru y 1958

during remissions *occurring on a maintenance schedule of* 100 150 mg daily Depression was less marked in males than in females because the gonadal part of the 17 ketosteroid excretion in the male is not subject to depression by cortisone Depression did not occur when cortisone was alternated with ACTH Combined ACTH and cortisone therapy initially had no inhibiting effect on 17 ketosteroid excretion because *of the corticotropic action of ACTH* In later stage extreme oscillations occurred apparently due to an antagonism between the stimulating effect of ACTH and the inhibiting effect of cortisone

The pattern of 17 ketosteroid excretion depended only on the hormone treatment and not on the severity of the disease However 17 ketosteroid titers were lower in cases of *relapse than in first attacks* This was *apparently due to* exhaustion of the adrenal gland caused either by the disease or treatment Spontaneous recovery of an exhausted adrenal gland was evidenced by a sudden increase in 17 ketosteroid excretion but a decrease to zero sometimes occurred despite energetic ACTH treatment indicating complete exhaustion of both adrenal glands

A *paradoxical pattern of 17 ketosteroid excretion* was encountered in some patients who received massive doses of cortisone (up to 900 mg daily) resulting in extremely high 17 ketosteroid excretion This also occurred sometimes in patients receiving cortisone alone after being previously stimulated by ACTH This paradoxical reaction could be explained as due to a change in the metabolic processes in the adrenal gland and the liver by which a high ratio of the cortisone administered was converted into 17 ketosteroid as long as the adrenal gland was completely suppressed

The pattern of 17 hydroxysteroid excretion examined in 9 patients was *fairly uniform Normal values were 2 12 mg* daily When treatment with cortisone and/or ACTH was started these values went up immediately eventually representing an excretion of up to 40% of the cortisone administered It seem therefore that up to this amount the drug may be excreted as tetrahydrocortisone in the urine

It is evident that neither 17 keto teroid nor 17 hydroxy corticoid excretion provides a reliable diagnostic or prognostic aid in pemphigus vulgaris Therapeutically low 17

ketosteroid values are a useful guide since they indicate when and at what dosage addition of ACTH to the routine cortisone treatment becomes necessary

The data allow interesting insight into the complicated mechanism of the ACTH cortisone relation and its manifestations in pemphigus especially in the later stages when exhaustion of the adrenal glands becomes unavoidable The authors experience shows that the result of such exhaustion is never complete atrophy of the adrenal gland but a periodic unresponsiveness which eventually results in spontaneous recovery A rapid method of determining 17 ketosteroid excretion in these cases would allow early diagnosis of impending exhaustion and permit well timed prevention by addition of appropriate doses of ACTH to the cortisone schedule

► [There are two school of thought about th desirability of giving ACTH simultaneously with cortisone or its analogues According to one school it is useless to administer ACTH while the patient is receiving oral cortisone because of the suppression of adrenal cortical activity produced by the cortisone Also current concepts suggest that pituitary gland function is depre sed by the administration of ACTH and this in turn further reduces adrenal cortical function The other school feels it is worth while to administer ACTH regularly as it prevents the adrenal cortex from becoming completely suppressed even though cortisone is being given by mouth The findings of Dostrovsky and Sulman support the latter viewpoint and provide a guide as to when it is desirable to add ACTH injections while cortisone is be g given orally —Eds]

Appraisal of New Antipruritic Trimeprazine (Temaril) Lawrence C Goldberg and Adrian Diamond[1] (Cincinnati) treated 160 patients with pruritus associated with dermatitis and systemic di orders Dosage of trimeprazine ranged from 2 5 mg twice a day to 5 mg every 3 hours Some patients with chronic diseases took the drug continuously for 6 weeks In over 70% of the patients relief from pruritus ranged from good to excellent The most outstanding results were in 32 patients with chickenpox none of whom had severe pruritus while taking the drug The drug did not affect any of the dermato es except to make them more amenable to routine therapy through decrease of itching This was particularly true of patients with atopic dermatitis

The commonest side effect was drowsiness noted in 60% of the patients which was controlled by adjusting the dosage One patient had giant urticarial lesions 24 hours after taking the drug and the same effect was noted when the drug

(1) A M A Arch Dermat & Clin Therap 5 58 584 September 1958

was tried again. Agitation was noted by 3 patients and a bad taste after taking the tablets by 1.

New Oral Antipruritic. Paul L. Williams[9] (Seattle) treated 90 patients who had severe pruritus complicating acute and chronic dermatoses and systemic diseases with trimeprazine (Temaril), a phenothiazine derivative. The usual starting dose was 2.5 mg. 3 or 4 times daily. Once the severe itching was controlled, the total daily maintenance dose needed was reduced to 5 mg. When nighttime itching was severe, a dose larger than the usual daytime dose was taken before retiring. Treatment lasted a few days to several weeks in acute cases and several months in some chronic cases.

Satisfactory results (complete relief from pruritus) were achieved in 75.5% of cases. Of 22 patients who had unsatisfactory results, 14 obtained complete relief from itching but also had side effects and 8 had incomplete relief from itching. The antipruritic effect of trimeprazine generally began 1-3 hours after the first dose was taken. Of 81 patients with severe nocturnal itching, 83% could sleep without interruption while taking the drug. Of 75 patients who had skin lesions at the time treatment with trimeprazine was started, 44 had complete healing and 20 had almost complete healing when the drug was discontinued. In 4 patients some evidence of healing was evident and in 7 no effect on the skin lesions could be detected though pruritus had stopped.

Side effects due to trimeprazine included drowsiness in 11 patients and lethargy, nightmares and a nonspecific skin eruption in 1 each. None were serious. There was no evidence of tolerance in any patient and therapeutic paradox was not observed. Occasionally, moderate hypotensive reactions were seen in patients receiving 20 mg. or more trimeprazine daily and antihypertensive drugs. Such large doses were rarely required, however.

► [Trimeprazine is well worth trying in the management of pruritus, bearing in mind that the soporific effect is quite marked for some patients. In our own experience, beneficial results were achieved somewhat less often than reported by Williams or Goldberg and Diamond. In view of its chemical structure, there is a possibility that it may cause photosensitization similar to chlorpromazine and Phenergan®, but thus far we have not seen or heard of any proved cases. A possible exception is a boy aged 3 who repeatedly developed blinking of the eyelids, apparently due to photophobia, when he was taking trimeprazine. The blinking disappeared each time the drug was stopped.—Eds.]

(9) Northwest Med. 58: 1161, September, 1959.

Oral Treatment of Keloids Edward W Kelly Jr and Hermann Pinkus[3] (Wayne State Univ) report experiences in treatment of 45 consecutive patients To rule out spontaneous regressive changes in hypertrophic scars no keloids of less than 6 months duration were included Many patients had had keloids for several years 1 had had large lesion for 40 years Dosage was 30 180 mg tetrahydroxyquinone daily

There was some favorable influence in every case usually manifested first by a fairly prompt lessening of tension pain and pruritus Objective regression of lesions was slow but definite In long standing keloid partial involution continued slowly over several years Younger lesions tended to respond more rapidly in 3 cases involution was complete Some lesions continued to regress after withdrawal of the drug There has been no recrudescence Follow up in some cases has been 5 years

In several cases histopathologic change were studied by repeated biopsy In earlier sections the collagen bundles appeared to be breaking up After treatment for 2½ years there were fewer coarse bundles and those that remained were frayed and the fibers were wavy Fixed connective tissue cells showed a relative or actual increase in number Reticulum fibers became more evident as the collagen bundle decreased in size Metachromasia decreased under therapy whereas staining with the periodic acid Schiff procedure increased indicating changes in the ground substance Mast cells increased in number especially those with granule taining with periodic acid Schiff reagent Melanocytes appeared to increase in size and seemed to have more and larger dendrite

Oral treatment of keloids with tetrahydroxyquinone leave much to be desired It is tedious and slow and the effect i incomplete in large lesions It has however caused ome regression in keloids of up to 40 years duration No side effect or untoward reactions have been observed and the drug has proved nontoxic in animals even in large doses The only undesirable reaction has been occasional local breakdown of keloid tissue accompanied by *discharge of necrotic material* This apparently is due to oftening of tis

3) A M A Arch Dermat 78 348 35 September 1958

sue around old devitalized collagen and is a sign of the effectiveness of treatment

Evaluation of the changes found histopathologically is difficult The increased amount of reticulum in the treated keloid and the number and relation of the fixed tissue cells bear some similarity to conditions in fetal skin The collagen in the regressing lesion is wavy similar to fetal collagen The mast cells however are poorly developed in fetal skin, whereas they are numerous and well granulated in the treated keloid

Softening of treated lesions is evident on palpation and in the greater ease with which local anesthetics can be injected The action of tetrahydroxyquinone is selective Normal skin of persons under treatment shows none of the changes seen in the treated keloid The exact mechanism of action of the drug is unknown Alteration of redox potentials in the tissue is a possibility as is action on enzyme systems

► [A radically different and new approach to the treatment of keloids Although this form of therapy may be prolonged it is noteworthy that keloids of 40 years duration responded to some extent A trial of injection of this compound into and around the keloid is a logical next step provided that the chemical does not produce undesirable local effects—Eds]

Scleroderma (Acrosclerosis)—*Treatment of three cases of noncalcific variety by chelation (EDTA)*—Chelate compounds are essentially coordinate compounds with the coordinate bonds arising from the sharing of an electron pair between the ion or atom of a metal and an ion or atom in the complex forming structure (ligand) The most common electron donating or electron sharing atoms in ligand molecules are nitrogen oxygen and sulfur When two bonding groups are present with proper spatial orientation in a single molecule a heterocyclic ring involving the metal ion may be formed in contrast to a complex which exists in a nonring form The formation of these rings is of utmost biologic importance in that they confer behavior properties on both the chelated metal and the ligands not previously characteristic of either alone

John G Rukavina Charles Mendel on J M Price R R Brown and S A M Johnson[4] (Univ of Wisconsin) treated 3 patients with noncalcific scleroderma (acrosclerosis) with a chelating agent disodium ethylenediamine tetraacetic

(4) J Invest Dermat 9 2 3 88 October 1957

acid (Na EDTA) Lessened induration and shininess of the skin particularly in the face neck and upper arms was definite Similar though less pronounced changes occurred in the skin of the hands There was increased mobility of the larger joints but joint deformities of the hands were little influenced by therapy Ulcers of hands and feet healed faster with concomitant diminution of pain

Several possible mechanisms of action of this drug are discussed Though EDTA exerts its most profound effect on the richest deposit of calcium in the body in the bone it may be that its impact on calcium in connective tissue (which may be abnormally laden with calcium in scleroderma) is even more significant in patients with this disease Another possible mechanism of action of Na EDTA is modification of the little understood magnesium calcium interrelation Finally the introduction into the body of this unnatural polyamine polycarboxylic acid might result in changes in no way related to its chelating properties

Experimental and speculative evidence seems to indicate there are several mechanisms by which a chelating compound may influence cells sequestration of unwanted metals removal of metals from intact organisms reaction with fixed intracellular metals catalysis tissue ligand extraneous metal relation and improvement of absorption Isolated examples of some of these mechanisms are known to the clinician viz BAL wherein toxic metals are removed from organisms by production of a less toxic chelate and nickel eczema in which a diet rich in citrus fruits leads to excretion of chelate complexes

Toxicity and side effect data in humans treated with EDTA though scarce nevertheless point to the possibility that in certain cases the treatment program may have serious consequences Severe damage to the kidneys hemorrhagic manifestations skin and mucous membrane reactions calcium embolism nausea and diarrhea have been reported Toxic manifestations are markedly reduced by oral administration of pyridoxine The recommended adult daily dose of Na EDTA is 50 mg/kg with a maximum daily dose of 5 Gm The drug is given intravenously dissolved in 500 cc of 5% glucose in water or normal saline The infusion should take 4 hours A suggested course consists in infusing the

drug for 5 days with a 2 day rest and repeating the cycle 3 times. After an interval of several weeks the course may be repeated if indicated.

II. Tryptophan metabolism before and during treatment by chelation (EDTA).—Price, Brown, Rukavina, Mendelson and Johnson found 3 female patients with scleroderma to have abnormal tryptophan metabolism characterized by an abnormally large urinary excretion of kynurenine, hydroxykynurenine, kynurenic acid and N-acetylkynurenine. The subjects excreted normal amounts of xanthurenic acid before and after ingestion of loading doses of l-tryptophan.

During therapy with Na_2EDTA the tryptophan metabolism became nearly normal in 1 patient and normal in another. Simultaneous administration of Na_2EDTA and pyridoxine considerably improved tryptophan metabolism in the subject who was the less responsive to Na_2EDTA alone. During a second course of Na_2EDTA both subjects responded as in the first trial. A third patient had normal tryptophan metabolism after treatment with Na_2EDTA or pyridoxine.

The authors explain the biochemical data on tryptophan metabolism in these 3 patients. In scleroderma there was abnormal urinary excretion of kynurenine and its metabolites after oral administration of tryptophan. Administration of pyridoxine or pyridoxine plus nicotinamide partly corrected the metabolic abnormality. The efficacy of pyridoxine plus Na_2EDTA could be explained on the basis of a decrease in tissue calcium, zinc and possibly other cations, making it possible for the metal ions normally functioning with pyridoxal phosphate to be used more advantageously. The data in the literature suggest that this metal which is unblocked for normal function may be magnesium.

► [In view of the report of Zarafonetis the abnormal tryptophan metabolism characterized by an abnormally large urinary excretion of kynurenine and related compounds is of particular interest. It is assumed that 5-hydroxytryptamine arises from the metabolic oxidation of tryptamine, the decarboxylation product of tryptophan.—Ed.]

Use of Relaxin in Treatment of Scleroderma. Guy C. Casten and Robert J. Boucek[6] (Univ. of Miami) treated 23 patients with scleroderma for 6-30 months with parenteral injections of the hormone relaxin. Relaxin in saline solution was given

(5) J. Invest. Dermat. 29: 89-99, October, 1957.
(6) J.A.M.A. 166: 319-324, Jan. 25, 1958.

subcutaneously in doses of 20 mg daily for 1 2 weeks and then the slowly ab orbed gelatin preparation was given in tramuscularly 10 mg daily Conjugated e trogenic sub stance (Premarin*) wa administered orally in do es of 1 25 mg daily for 2 weeks before or simultaneous with the in ti tution of relaxin therapy

Of 21 patients with a significant degree of Raynaud s phe nomenon 18 noted improvement after treatment for 3 5 week Improvement occurred in 14 of 18 patients with tro phic ulcer Complete healing of the ulcers occurred in mo t patients Softening and loosening of the skin particularly of the face and upper extremities was noted by 16 of 22 pa tients with generalized skin tightness The skin of the hand and feet was not altered significantly

Withdrawal of relaxin caused a return within 3 10 days of Raynaud phenomenon and skin tightness Symptoms seemed to return in a more severe state than before therapy but in all cases responded favorably to subsequent relaxin administration Other manifestations of scleroderma such a renal pulmonary or myocardial failure were unaltered by relaxin treatment To maintain the effects of the hormone it wa nece ary to administer it daily or every other day

Side effects were not of major importance In 3 women menorrhagia occurred during the first few men trual periods after on et of therapy Treatment was either discontinued or the dose reduced during the menorrhagia One patient had distressing local reactions to the injections and refu ed fur ther treatment Three noted weakness and in 1 this symptom wa o evere that treatment was di continued

Relaxin influences connective tissue other than that found in and around the genital tract The response of the vaso spastic feature of the disea e Raynaud phenomenon to the hormone ugge t that a vasodilator effect may be operating The character of thi reaction is unknown but may be re lated to the action of relaxin on the mast cell Re pon e of trophic ulceration may be related to depolymerization of the ground ub tance in connective tissue which might per mit more rapid diffusion of substances from the vascular tree Further skin nutrition may be improved by an increa e of its vascular supply re ulting from amelioration of vaso pa m Loo ening of the kin of patient with cleroderma

may be related to the action of relaxin on the collagen fiber

► [On the basis of personal communications from others it is our impression that relaxin is useful principally to promote healing of the ulcers in acrosclerosis but that it has very little if any effect on the sclerodermatous cutaneous changes.—Eds.]

Intravenous Procaine in Management of Some Cutaneous Manifestations of Collagen Diseases was used by Joseph Farrington (Jacksonville, Fla.). Each patient was hospitalized, then prepared by administration of Seconal® 0.1 Gm. orally 20 minutes before starting intravenous therapy. The initial dose consisted of 500 cc. of 0.1% procaine in normal saline or 5% glucose solution. If there were no untoward reactions, the patient was given 1,000 cc. once a day for the next 6 days at 45 drops/minute. Such courses were repeated at intervals of 6 weeks until optimum improvement was obtained. If there was no additional improvement after the third course, therapy was discontinued. The maximum number of courses given any one patient was 12. No serious side effects were observed.

Of 71 patients with scleroderma of all types who were treated, in about half the condition was acroscleroderma or generalized. Improvement varied in degree but seemed permanent. There was softening of the skin in most; soreness, stiffness and swelling of the joints improved. Raynaud's phenomenon, present in 8 patients with acroscleroderma, responded dramatically in 6. The sharp borders of localized scleroderma usually at the end of 6 weeks would begin to blend imperceptibly into the surrounding skin with gradual disappearance of the lilac halo. Of 71 patients with all types of scleroderma encountered over 7 years, only 2 died. These were young women who were moribund before receiving intravenous procaine. In 3 patients with dermatomyositis and severe Raynaud's phenomenon, vasomotor symptoms were relieved by procaine treatment.

The author had hoped that by relieving the confines of a "hide-bound" epidermis in patients with scleroderma or dermatomyositis the underlying musculature would over a period regain its normal size and development. However, muscular atrophy persisted apparently unchanged long after the overlying skin became soft and pliable.

► [Any method which does not produce serious side effects but yet may

(7) South. M. J. 51: 14[illegible]-1431, November, 1[illegible]8.

be of aid to some patients is worthy of trial in scleroderma where ordinarily so little can be done to help —Ed]

Treatment of Psoriasis with Riboflavin Bencel L Schiff and Arthur B Kern[8] (Boston Univ) treated 90 patients who had chronic psoriasis Weekly injections of 1 cc of aqueous solution containing 50 mg riboflavin 5 phosphate sodium (equivalent to 35 mg riboflavin) was given to 77 patients for 1-4 months 40 of these also received riboflavin orally 7 5 mg 3 times daily Thirteen patients received 1 cc riboflavin solution intramuscularly daily for 4 months

Of the 90 patients 33 showed some improvement Relief from itching was noted in some of the 57 who showed no objective improvement Patients who received daily injections showed no greater benefit than those who received weekly injections The addition of oral treatment failed to have any demonstrable effect The authors conclude that riboflavin has little value in treating psoriasis

► [We agree – Ed]

Sulfonylurea Derivatives in Treatment of Psoriasis Vulgaris Preliminary Report G Kabelitz and W Kappel[9] changed the treatment in 2 diabetic patients with psoriasis from insulin to Artosin a benzinesulfonylurea derivative After 3-4 weeks treatment with 0 5 1 Gm Artosin daily the psoriasis improved considerably Trial of Artosin in 25 more psoriatic patients without diabetes led to healing or great improvement in 17 during a follow up of 6 12 months Only far advanced and extensive psoriasis responded to Artosin Response was independent of age sex or age at onset of the disease A hypoglycemic reaction which required discontinuance of the medication occurred only once In mild reaction temporary reduction of the dose sufficed

The effective dose of Artosin is 0 5 1 Gm daily in 2 divided doses Improvement can be expected in 15 20 days Medication must be continued until cure is effected or there is great improvement Thereafter a smaller maintenance dose is advisable A relapse calls for a new course of Artosin The mode of action of the drug in psoriasis is unknown

Treatment of Psoriasis with Folic Acid Antagonists Walter F Edmundson and William B Guy[1] (Pittsburgh) treated 62 patients with moderate to severe psoriasis with

(8) A M A Arch Derm 78 643 November 1958
(9) Deutsch med Wchnschr 83 1167 July 4 1958
(1) A M A Arch Derm 78 200 03 August 1958

aminopterin amethopterin or both The dosage of aminopterin was 0 5 mg daily for 6 days withdrawal for 3 days and 0 5 mg daily for 6 days Amethopterin was given in the same manner in dosage of 2 5 mg daily for a total of 30 mg in 12 doses Some patients were treated further with 0 5 mg aminopterin or 2 5 mg amethopterin daily for 9 days administered 3 weeks after the original course Repetition of a course of 12 doses was not prescribed until 3 or more months after the original therapy The rest periods probably reduced the cumulative toxic effects of the drugs In this series mild toxic effects were rarely observed and there were no serious untoward reactions

Aminopterin was given to 52 patients 17 received amethopterin and 13 received both drugs Aminopterin in doses of 0 5 mg gave almost identical clinical results as amethopterin in 2 5 mg doses Of those patients who received only one of the drugs 75% had over 50% improvement at the time of the last observation period which in several cases was more than 6 months after treatment Of the 13 patients who received both drugs 11 maintained more than 50% improvement until the last observation date

The relatively low and almost nontoxic dosage schedule used appears to be practical for treatment of moderately severe or severe cases of psoriasis although the clinician must be alert to toxic effects and drug idiosyncrasy which may occur in any patient taking folic acid antagonist Because of the toxic effect on fetal tissues it is probably best not to give the drugs to women during the childbearing age

► [One can draw the conclusion from this article that as reported by Lee Bennett and Pollack aminopterin and amethopterin proved beneficial in many cases of psoriasis and that they do not produce immediate toxic effects of consequence in the conservative doses used As has been pointed out on many occasions in the past patients receiving these folic acid antagonists should have careful medical follow up including repeated blood count

Besides the folic acid antagonists most patients in this study used topically a mercury soap in motor oil mixture and received injection of 1 000 µg vitamin B or 35 mg riboflavin every 2 weeks for about 3 months after their course of treatment These were given to provide post treatment observation —Ed]

Effect of Cycloserine on Skin Tuberculosis Preliminary Report is made by Juvenal Esteves (Univ of Lisbon) Cycloserine is a new wide spectrum antibiotic which is ob

(1 JI Barret 8 494 496 November 195

tained from various streptomyces species It was first used in patients who were resistant to streptomycin and isoniazid

The author tried cycloserine in 22 patients with skin tuberculosis (2 had lupus vulgaris and 20 erythema induratum Bazin and papulonecrotic tuberculids) The daily administration of 0 75 1 Gm led to clearing of tuberculid type skin changes in 8-60 days in 18 patients who tolerated the drug well In 2 the drug had to be discontinued right at the beginning because of severe side effects In 4 relapses occurred between 2 and 8 weeks

The therapeutic effect was relatively uniform quick and independent of previously given treatments The blood sedimentation rate usually became normal when the patient improved clinically In lupus vulgaris cycloserine given in the above amounts for 2 months did not have any clinical or histologic effect on the granuloma The discrepancy between the good result in patients with tuberculids and the poor results in those with lupus vulgaris if confirmed by further studies might throw some light on the possible organotropic mode of action of cycloserine

Treatment of Leprosy with Cycloserine an antibiotic obtained from cultures of Streptomyces orchidaceus garyphalus and lavendulae and also synthetically was assayed in 1[?] patient by V Pardo Castello[3] (Univ of Havana) The drug previously was used to treat tuberculosis Some of the patients had had no previous treatment and others had been treated for varying periods with diaminodiphenylsulfone with unsatisfactory results or no effect

The dosage of d cycloserine (d-4 amino 3 isoxazolidinone used was 500 1 000 mg /day in tablets of 250 mg taken with a glass of water The larger doses of 1 Gm produced at times gastrointestinal and general symptoms and hence were reduced to 2 or 3 tablets daily (500-750 mg) Tolerance in a[ll] was good without renal hepatic or hematologic complications The patients remained in good general health and blood pressure, arterial pressure and psychic state were normal

The results of treatment which lasted from 3 to 15 months were favorable with slow progressive clinical improvement in cutaneous and mucosal lesions *similar to that seen wi*[th]

[3] [illegible] 15 16 [illegible] 19[?]8

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(3) *Hs* [illegible] 8 494-496 November 195[illegible]

romas This lighter appearance signifies beginning resorp tion Simultaneously hypertrophy of the leprosy cells can be observed which increase their volume two to three times without revealing any structural changes

With progressive treatment early in the 2d year when the drug effect on the leprosy bacilli becomes more intensive a large number of Virchow cells show various changes the meshwork of the intraprotoplasmatic reticulum begins to tear and coalesce Later these intracellular changes affect more and more Virchow cells

The resorptive processes are not always uniform often there are zones with far advanced healing besides areas of unchanged infiltrations The resorption usually proceeds from deep to superficial areas beginning in the subcutis

In the course of lepromatous leprosy the lymph nodes are constantly involved the inguinal femoral and cervical nodes are most commonly involved The successive histo logic changes in the lymph nodes under sulfone treatment are similar to those seen in the skin

Most of the leprosy bacilli are found in the histiocytic cells Inside these leprosy cells (or Virchow cells) the bacilli multiply vigorously fill the entire cell and remain there for a long time During the first months of sulfone treatment even before histologic changes become apparent the bacteria become fewer and appear granular Toward the end of the 2d treatment year all the bacilli not only appear granular but change their characteristic pattern of grouping Simultane ous with the advanced cellular destruction the bacilli dis appear from the cells by dissolution Some still remain inside the cells whereas others are expelled into the surrounding tissues where they appear as isolated granular rods With progressive treatment these rods di integrate into masses of fuch in ophil or even cyanophil granules Leprosy bacilli resist treatment longer in the lymph nodes than in the skin Therefore the sterilization of the lymph nodes can be con sidered the mo t important test of cure

Sulfamethoxypyridazine in Dermatitis Herpetiformis J Jefferson (Belfast) reports satisfactory response in the treatment of 12 patients One patient had a severe bullous eruption and 4 had the juvenile type of dermatitis herpeti

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sulfone treatment There was little change in microscopic findings despite intense and prolonged treatment Acid fast bacilli of Hansen were investigated weekly at first and later every 2 weeks or monthly these were demonstrable in all cases but with some favorable changes, i e, *signs of degeneration in both cutaneous and nasal mucosal lesions*

Clinically the improvement was as marked as that with diaminodiphenylsulfones *Lepromas softened faded and* were absorbed infiltrative lesions of the palatal and laryngeal mucosa were reduced within a few weeks and finally flattened into red or reddish macular lesions and diffuse cutaneous infiltrations were reduced in size and remained as reddish erythemas which later faded and disappeared slowly In 2 cases in which diaminodiphenylsulfone apparently yielded no benefit cycloserine gave favorable results clinically permitting 1 patient to resume his professional activities *without any sign of the disease* Treatment had to be suspended in 1 patient because of psychic disturbances which were probably not caused by the medication since *psychiatric investigation revealed a mentally disturbed* individual

Cycloserine is an excellent addition to antileprous therapy and deserves a large scale trial in doses not exceeding 750 1 000 mg /day

Histologic and Bacteriologic Changes in Lepromatous Leprosy *after Treatment* with Diaminodiphenylsulfone (Sulfone Parent Substance) St G Nicolau and P Vulcan[4] (Therapeutic Inst of Roumanian Academy of Sciences Bucharest) treated successfully with diaminodiphenylsulfone 120 patients who had lepromatous leprosy The histologic and bacteriologic changes which took place in the slowly healing and finally disappearing skin lesions were studied The histologic changes *began during the 2d month but* became pronounced during the 4th and 5th months of treatment *Thereafter a slowly progressive but steady resorption* of the lepromatous changes could be observed Complete resorption took about 2½ 3 years or more

Biopsy specimens of lepromas taken at regular intervals during treatment, showed first a lighter appearance of part or all the infiltration—in striking *contrast to untreated lep*

(4) Arch klin u exper Dermat 0 486-498 1958

a high inherent error Among the consideration that determine a patient s answers to questions in complex situations are (1) the actual pharmacologic effect of the agent under test (2) ignorance or disbelief that a placebo was or might have been used (3) do e of the active agent (4) ancillary cue such a gastric irritation to the active agents (5) specificity efficacy and con picuousnes of re ponse to the active agent (6) problems of semantic interpretation of both questions and answers (7) nature of the questions asked with particular regard to a tendency to suggest or to inhibit a particular answer (8) efficacy of concurrent therapeutic agents or other changes in the patient s environment including passage of time and (9) the base line against which the patient must make comparison

► [This stu ly seems to prove principally two items (1) the high inherent testimon al error a it is called by the authors which must be reckoned with in such stud es and (2) the failure of 8 methoxypsoralen (Meloxine) to s gnificantly change the sunburn and sun tan reactions of the subject tudied under the conditions of the tests This drug was re l ased with the claim that in doses of 20 mg it protects against sunburn and increases kin pigmentation The authors administered 10 70 mg with ry uncon incing result Therefore we feel that at present such claims e unwarranted It seems to us that from a public health viewpoint der atologists h uld explain why the pul l c should *not* sun bathe and sun tan exc ssi ly thus discouraging overexposure The promotion of Melox a sunl urn prevention and sun tanning agent does exactly the oppo te it encourages even more sun expo ure —Eds]

Effect of Diphemanil Methylsulfate (Prantal*) on Hyperhidrosis of varying degree in 51 patients was investigated by Norman Orentreich and Charles Robert Rein (New York Univ Po t Grad Med School and Skin and Cancer Unit) Schedules varying from 50 to 400 mg 1-4 times daily were used As the effects were determined patients adjusted the lo age chedule to individual need The effect of an adequate do e of diphemanil methylsulfate was apparent in 30 minute and lasted 4 5 hours there were no permanent effect Generally the higher the dose the more effective it wa f r hyperhidrosi and the more side effects it produced

Of the 51 patient response was excellent in 13 good in 28 and moderate in 7 The average dose required for good results was 200 mg every 4-6 hour Xerostomia occurred in 21 patient it wa minimal in 4 mild in 8 moderate in 5 and severe in 4 Other side effects noted were bitter taste tin

A M A Arch Derm t 6 65 December 19

formis One adult and 3 children remained well after cessation of treatment

Most adult patients received 3 or 4 sulfamethoxypyridazine tablets daily for 1 to several weeks until the eruption cleared Maintenance dose was 1 or 2 tablets daily in most though some patients required 3 or even 4 tablets to prevent recurrence of lesions Dosages were lower in children

In view of the variable course of dermatitis herpetiformis and the possibility of spontaneous remissions it is difficult to assess the results of treatment All these patients however responded immediately In 2 cases treatment was interrupted when supplies were temporarily held up In each the eruption promptly recurred and rapidly disappeared when treatment was resumed

Toxic symptoms were almost entirely absent despite the comparatively large doses of sulfamethoxypyridazine One patient had what appeared to be genuine rubella and continued treatment without ill effect Another had dizziness and headache but was able to continue the necessary dosage without further reactions One patient has been taking 4 tablets daily for over a year without side effects Blood counts and urine have remained normal

► [The incidence of drug eruptions among patients treated with sulfamethoxypyridazine (Kynex®) has been rather high and some have been serious (this YEAR BOOK p 182) This would seem to preclude wide use of the drug in a chronic disease such as dermatitis herpetiformis —Ed]

Effects of Oral Methoxsalen (8 Methoxypsoralen) on Sunburn and Sun Tan Blind Clinical Trial Farrington Daniel Jr Carl E Hopkins and Thomas B Fitzpatrick[6] (Univ of Oregon) report that a double blind controlled study of reactions of 106 patients using methoxsalen (10 20 mg daily) and an identical placebo failed to show that these patients could discriminate between lactose placebos and methoxsalen as to sunburning and tanning effects A significant relation was found between the patient s statements of his usual tendency to sunburn and his claimed protection from sunburn while using the blind placebo

Since methoxsalen is a known potent photodynamic agent the point of the authors study is not that patients are reacting falsely to an inactive agent but that testimonial data have

(6) A M A Arch Derm at 77 50150 Ma 1958

In all patients besides the reserpine fomentations of aluminum subacetate (1%) and an ointment of equal parts zinc oxide talc glycerin and distilled water were given As controls some patients received identical local medication and antihistamines Comparative studies showed definite control of pruritus in those treated with reserpine control was inconsistent in those treated with antihistamines No side effects were noted with reserpine except in 1 patient who had headaches on 0 75 mg daily The satisfactory tolerance may be attributed to the low doses used The average of 0 375 mg was much less than others have used in treatment of other dermatoses (to 4 mg)

On the basis of the favorable results obtained in this series reserpine deserves wider trial in treatment of eczema of the legs due to vascular insufficiency

► [It is difficult to assess accurately these results obtained with reserpine in eczema of the legs since no placebo medication was given to the subjects who were benefited However there are several possible explanations as to how a reduction in itching may occur under reserpine medication (1) the general tranquilizing effect (2) a central nervous system effect as on the diencephalon (3) sympathicolytic lowering of blood pressure or other pharmacologic actions and (4) an effect on the mast cells in the skin The last mentioned possibility must be considered in view of the peculiar effects observed by Bersani Pelzig and the senior editor in 3 patients with urticaria pigmentosa who received reserpine—Eds]

Treatment of Chromoblastomycosis with Calciferol is discussed by Clovis Bopp[9] Surgical or electrosurgical treatment of chromoblastomycosis is often followed by relapse or the appearance of metastatic lesions An apparent explanation is that surgical procedures often open the fibrous barrier in the deep corium which tends to keep the fungus localized to the upper corium and epidermis The only exception to this is the method of Farina in which a wide and deep excision down to the aponeurosis is followed by skin grafts However this method is only practicable for lesions of limited extent

Treatment with calciferol combined with iodides may be considered the first rational treatment of this disorder The author has used three plans of treatment which were developed successively as experience demonstrated the disadvantages of previous plans Under the first plan oral calciferol was given in 600 000 unit doses every other day for 30 80

(9) Of G f La ra d Globo P rt Al g Bra 1 1957

gling of the tongue, "gas" in the stomach, nausea and dry nose. No difficulties with accommodation were noted.

Determinations of the diphemanil methylsulfate-methantheline (Banthine®) antisweating pharmacologic ratio were made in 12 patients. The weight for weight ratio was about 4:1 (200 mg. diphemanil being equal to 50 mg. methantheline) in 6 patients and over 2:1 in the other 6. Xerostomia occurred in 75% of the patients taking methantheline.

A review of the literature revealed that some failures to achieve uniform results with the quaternary amines were due to inadequate dosage, uncontrolled variations in dosage schedules and lack of provision for variations in patients' response to these drugs.

► [We also have had favorable experience with diphemanil methylsulfate in some patients, but in others the side effects with any anticholinergic drug are so disagreeable that the patient prefers the hyperhidrosis.—Ed.]

Antipruriginous Effect of Reserpine in Eczema of Legs was studied in 23 patients by David Grinspan and Jorge Mulhafra[8] (Buenos Aires). Eczema of the legs in patients with venous insufficiency is difficult to treat and frequently recurs. Although appropriate local treatment often produces improvement with decrease in pruritus, this may not disappear entirely. A vicious circle is then established: persistence of pruritus and consequent scratching exacerbates the eczema, which in turn increases itching. Under such conditions antihistamines and older antipruriginous remedies (calcium, magnesium hyposulfite, peptone, etc.) usually fail. Barbiturates and other sedatives carry the risk of sensitization and drug allergy which would make the dermatosis worse. Further, they have no significant effect. Corticoids and ACTH are expensive and require special caution if used for some time.

In the 23 patients (16 women) treated with reserpine, eczema of the legs was secondary to venous insufficiency, although actually the eczema was of microbial origin. The amount used varied between 0.25 mg. in 2 doses and 0.75 mg. in 3 doses. In most, 3 doses of 0.125 mg. (0.375 mg. daily) were sufficient. Results with respect to pruritus were excellent in 14 patients (10 women) and good in 9 (6 women). In 17, the effect was immediate, and in 6 relief appeared after 5-10 days. Maximum duration of treatment was 45 days.

(8) Arch. argent. dermat. 7: 367-372, December, 1957.

Calciferol eem only to stimulate the ame defen e reac tion which the host normally develops to circumscribe and dominate the invading organism Without showing apparent fungistatic or fungicidal effect calciferol enhances the prolif eration of fibrous tissue and reduces the cellular infiltra tion It probably has the same biochemical action in chromo bla tomyco i that Charpy has de cribed in lupus vulgari namely production of tis ue acido is and enhancement of the hydrolytic action of alkaline pho phatase with liberation of pho phoric ion Others have hown that ti sue acidifica tion elicit connective tissue proliferation

Trial of Chloroquine in Treatment of Lichen Planus Veikko Lirila and Sirkka Helanen[1] (Univ of Helsinki) treated 35 patient Duration of the di ease before treatment was le than 3 months in 12 cases 3 6 months in 14 and more than 6 month in 9 The u ual do age was 0 250 Gm chloroquine daily but 11 patients received 0 5 Gm daily dur ing part of the treatment period Duration of treatment was 1 3 month in 15 ca e 3-6 months in 13 and over 6 months in 7 Side effect occurred in 9 patient One patient exhib ited a generalized erythroderma after 1 month of treatment 1 patient had mild leukopenia and the others had mild tran ient ymptoms including nau ea in omnia tiredne vertig and vi ual di turbance

After 6 m nth treatment 21 patients (60%) still had ac tive le ion The corre ponding figure in Samman s ca es of untreated lichen planu was 43% Only 3 of the pre ent 35 patient were free from le ion after a total duration of the di ea e f 6 m nth (including the period before and during treatment) and in 22 patient (63%) active le ions were till pre ent after the di ea e had been present 12 months Among Samman patient 27 till had le ion 12 months after n et

Thu the c ur e f lichen planu was more prolonged in patient treated with chloroquine than in untreated pa tient Th ugh the difference may be insignificant it i evi lent that chl roquine ha little or no beneficial effect on the ur e f the di ea e

► [Th egati e finding i prese ited he e since it may prevent other f m u g th f rm of treatment l chen pla u In wide pread ymp

[1] Acta d el 38 194 19 1 58

doses Occasionally, the course was repeated once or twice With this method some patients relapsed after initial improvement and many exhibited symptoms of overdosage In the second plan calciferol was given on alternate days for 2 6 weeks and then once a week for 30 40 doses No significant toxic effects were noted The third plan called for administration of calciferol in doses of 600 000 units weekly for 15 25 weeks No toxic effects were observed and the lesions flattened out more rapidly than with the other plans

In all three plans besides calciferol each patient received 1 3 Gm potassium or sodium iodide Compresses of Alibour or Thierch solution were also applied When exudation diminished most of the patients used Unna s zinc gelatin boot for 1 2 weeks

Of 14 patients treated by the first method 2 showed histologic cures in an average of 9 months and 8 showed clinical cures in an average of 7 months Four showed substantial clinical improvement and are still under observation after an average of 17 months Of 5 patients treated according to the second plan 1 was cured histologically after 6 month 3 were cured clinically in an average of 5 months and 1 has shown significant improvement after 6 months Of 5 patients treated by the third method 1 was a new patient and 4 had relapses following treatment by the first plan Two of the 5 were cured histologically in an average of 3 months 2 were clinically cured in an average of 3 month and 1 showed significant improvement after 2 months at which time he abandoned treatment

The host reaction to the fungus in chromoblastomycosis features several steps (1) development of dermal microabscesses containing numerous fungi (2) formation of dermoepidermal fistulous openings making possible the discharge of these suppurative foci to the exterior (3) development of a band of cornification in the malpighian layer giving rise to horn pearls containing cellular debris and fungi (4) granulomatous reaction in the dermis with formation of epithelioid nodules and destruction of encircled fungi and (5) formation of a fibrous barrier in the deep corium limiting the cellular infiltration while newly formed bundles of connective tissue cross the upper dermis in all directions tending to replace the infiltrate with scar tissue

definite but limited reduction in rhus sensitivity may be at tained by oral or intramuscular administration of rhus aller gens With rhus oleoresin maximum hyposensitization is obtained with about 2 000 2 500 mg intramuscularly and 2 500-3 000 mg orally With the pure but less potent penta decylcatechol this state is reached with about 2 500 3 000 mg intramuscularly and 3 500-4 000 mg orally

Hypo ensitization occurs in a definite pattern revealed by quantitative patch tests The reaction to the highest dilution declines first Only the end portion of the dosage response curve is notably affected A 100 fold decrease in titer is rare A given fraction of the original sensitivity may be abolished but no more regardless of the height of the total dose or the initial degree of ensitivity

Various sy temic and mucocutaneous side effects may ap pear in the cour e of hyposensitization They are attributa ble o far as present understanding goes entirely to allergic reactions The main signs and symptoms are mucocutane ou pruritus and flares of healed sites rashes dyshidrosis and urticaria Systemic reactions in this study were never met with con ervative oral prophylaxis Such reactions to intramuscular treatment were mild and infrequent with con ervative prophylaxis but severe and frightening with more vigorous treatment Systemic reactions included fever grippelike yndromes muscle aches asthenia meningismus bout of coughing and wheezing and headaches No anaphy lactoid reactions were ob erved

The blood cell which most sensitively reflects the impact of rally or parenterally admini tered rhu antigens in sen itized per on i the eosinophil Eosinophilia is an inevita ble development in every instance of clinical sensitization whether mild or strong in which large quantities of allergen have been given especially intr mu cularly With conserva tive ral prophylaxi eosinophilia is less intense and often ab ent Leukocyto is with white blood cell counts of 10 000 24 000 often accompanies intense eosinophilia and is in pro portion t it With conservative oral or intramuscular penta decylcatechol prophylaxis other changes in the peripheral bl od are uncommon

Hypo ensitization is not easily achieved in allergic con tact dermatiti One is confronted with the problem of giv

tomatic cases of lichen planus triamcinolone or other corticosteroid may be worth a therapeutic trial —Eds]

Vitamin B_{12} in Treatment of Congenital Ichthyosiform Erythroderma A Lodin, H Gentele and B Lagerholm (Karolinska Hosp Stockholm) treated 5 patients with congenital ichthyosiform erythroderma with extremely large doses of vitamin B_{12} (1 000 6 000 μg daily) intramuscularly combined with vitamin C (up to 1,500 mg daily) orally No other treatment was given concurrently Spontaneous remissions had not occurred previously in any patient Pronounced improvement was observed in all In 2 patients improvement did not begin until treatment had been given 2 3 weeks In 2 others improvement occurred with doses of 1 000 μg daily but the healing process ceased after several weeks of therapy Dosage was then increased in increments of 1 000 2 000 μg to a maximum of 6 000 μg daily With each increase in dosage improvement was again noted When treatment with vitamin B_{12} was stopped exacerbations occurred within a week or so The healing process was similar in all cases The first sign of improvement was detachment of the scales marginally Desquamation then occurred and the skin became paler and softer No side effects were observed with the massive dosage of vitamin B_{12} used

According to various investigators one function of ascorbic acid is that it plays a significant part in the conversion of folic acid to citrovorum factor Though the interaction of vitamin B_{12} and folic acid in cell metabolism and maturation is not completely understood some authors believe that vitamin B_{12} also participates in the formation of citrovorum factor from folic acid Vitamin B_{12} folic acid and citrovorum factor all take part in normal cell maturation Accordingly the authors administered a large adjuvant dose of vitamin C in the belief that it might reinforce the effect of vitamin B_{12}

► [In the 1 case in which this treatment was used by Dr H Gordon at the New York Skin and Cancer Unit similar results were achieved. Improvement was noted up to a point beyond which there was no further progress despite continuation of therapy —Eds]

Hyposensitization against Rhus Dermatitis is discussed by Albert M Kligman[3] (Univ of Pennsylvania) During 3 years many different schemes of hyposensitization were tried, more than 2 000 subjects participated in the study A

(2) Acta dermat venere 1 38 51 67 1958
(3) A M A Arch Dermat 78 47 7 July 1958

lyzed by P de Gracian ky and Ch Grupper[41] (Saint Louis Ho p Paris) Five had sero negative primary syphilis 29 sero positive primary syphilis 51 secondary syphilis (3 re infection) 8 gumma 9 tabes with or without meningeal reactions (arthropathy) 2 aortitis 3 gumma 1 and optic neuritis 1 5 aortic syphilis (2 with aneurysm) 3 serologic syphilis discovered during pregnancy 2 pure serologic syphilis 4 late congenital with interstitial keratitis and 4 known sensitivity to penicillin

At the beginning of the series cortisone was u ed intra mu cularly or by mouth for 5 days then 5 8 days (exception ally 30 day) 100 mg /day In 21 cases hydrocorti one 100 120 mg /day was given 5-6 days sometimes for 15 days In 2 case perfu ions of ACTH 25 mg in 500 cc glucose saline olution were tried Local corticotherapy was used as subconjunctival instillations or injections in interstitial ker atitis and intra articular injections of 1 5 cc hydrocortisone were given in arthropathic tabes In the last 30 cases delta 1 dehydrocorti one 30 mg /day was given for 6 days In the technic currently used the single penicillin injection is given the 4th or 5th day of the cortisone course

Corti one prevents or decreases in most instances the Herxheimer reaction both in acute and chronic cases Only 6% of the patients in this series had temperatures of 102 2 104 F following penicillin injection as contrasted with 50 80 / u ually reported when cortisone is not used

Clinical manife tation of syphilis including chancre secondary syphilids cutaneous and mucous gummas subjec tive symptoms due to neurologic involvement and intersti tial keratiti are modified by cortisone improvement varies with stage and severity of the lesion Cortisone significantly reduces pathologic evidence of activity with diminution or di appearance of treponema decreased concentration of re agin in primary and secondary syphili and in tertiary cases with clinical manifestations and lessening of abnormal find ings in erebrospinal fluid Conversely there is no change in reagin concentration when it is low in the so called specific er logic te ts Corti one does not diminish treponema sen sitivity to penicillin nor is the usual course of syphilis after penicillin treatment altered Cortisone is useful as an adju

41 Rev fra c et 1 1 t bi 1 2 579 594 1957

ing a large amount of allergen safely. Intramuscular prophylaxis is not feasible in clinical practice. Too many injections are required and, even with conservative dosage, adverse reactions are too numerous and severe. Oral prophylaxis is preferable. Doses can be advanced slowly by small increments. Signs of intolerance can be recognized early and intercepted. Pentadecylcatechol is theoretically advantageous because of its purity and stability. Unfortunately, its synthesis is somewhat costly and it will not be available in the immediate future.

The usual initial dose of pentadecylcatechol is 1 drop of a 10% alcoholic solution daily for a week. This is gradually increased: 2 drops are given daily the 2d week, etc. With oral prophylaxis, skin rashes and pruritus are the symptoms which most often prevent advancement of the doses in the prescribed manner. Some patients react even to 1 or 2 drops. This barrier can generally be overcome by daily administration of 50-100 mg. cortisone acetate or its equivalent, depending on the severity of the reaction. Even with cortisone the dosage must be cautious and personally regulated.

At present nothing is known about the mechanism of hyposensitization. Presumably, the allergen in some way combines with and binds antibody so that it is no longer available for reaction with allergen. Hyposensitization is temporary. It begins to wane after a few weeks. The original sensitivity is gradually regained within 6-10 months, occasionally longer. Maintenance dosage was incompletely studied. Five drops of 10% alcoholic solution of pentadecylcatechol daily by mouth was adequate maintenance in 20 subjects. Lower amounts were not investigated.

► [In this study Kligman confirms much of what was previously known besides revealing some interesting new data regarding hyposensitization to poison ivy. The relatively small differences in the quantities of allergen necessary for hyposensitization by the oral method (2,500-3,000 mg.) and intramuscular method (2,000-2,500 mg.) are notable, as are the hematologic changes (eosinophil and total leukocyte count).

Because it is stable and pure, pentadecylcatechol in one way would be advantageous for hyposensitization procedure. However, one must ask whether this very stability is not also a drawback because it is likely to make the compound immunologically nonaggressive as compared with the less stable unsaturated compound among the poison ivy allergens. —Eds.]

Cortisone and Syphilis: Results of Corticotherapy Preceding Course of Penicillin in 120 Cases of Syphilis were anu

ising agents in the treatment of syphilis but further evaluation seems indicated before recommendation of their wide spread use in treating this disease Tetracycline and synnematin B have recently been used successfully in treating a few ca es of early syphilis

► [For gen ral use penicillin remains the therapeutic agent of choice in syphilis However because of the increasing incidence of severe and dangerous reactions due to penicillin sensitivity it is important to know what other anti yphilitic antibiotics are available In these times when such a large proportion of the population has been previously exposed to penicillin it is wise to have at hand those materials which will be needed hould the patient have a systemic (anaphylactoid) reaction following penicillin injection —Ed]

C Physical Therapy

Radiation Protection in Dermatology Anthony Domonko and Gordon H Cameron[6] (New York) studied for several years the amount of radiation to which dermatologists and their assistants were exposed in active private practice The study was done in an office with 3 identical x ray machines of modern desig n a contact x ray apparatu 300 mg radium and thorium X in alcohol olution

The inherent filtration of x ray tubes and their housings was equivalent to approximately 1 mm Al The machines operated at 100 kv 7 ma target skin distance 30 cm and half value layer 1 4 mm Al The inherent filtration of the contact x ray tube and its housing was 0 15 mm Al and the machine operated at 45 kv 2 ma half value layer 0 3 mm Al and target skin distance 1 8 cm The radium supply was stored in a conventional safe in a cabinet with lead walls 3 2 in thick Thorium X was used for 2 days every week an average of 1 500 µc being used weekly

Film badges worn intermittently by all office personnel were changed at weekly intervals A total of 444 film badges was used In addition 2 pocket dosimeters were used by thre e e pecially concerned with radium therapy On the basis of measured scattered radiation from roentgen apparatus and direct radiation received from radium and thorium X correlated with amounts received by dermatologists and their personnel it was found that they were protected well

(6) A.M.A Arch Derm t 76 694 698 D embe 195

vant to relieve sharp pains and visceral crises of tabes arthropathies and interstitial keratitis When cortisone is given penicillin is tolerated better by allergic subjects and pregnant women and in patients with aortic and neurologic syphilis

Although some facts such as morphologic change in the treponema under the influence of cortisone alone their diminution and their earlier disappearance (as compared with controls) in primary or secondary lesions suggests a possible direct effect on the organisms the principal therapeutic effects of cortisone are attributed to changes in the host Effect on rate of circulating antibodies changes in specific infiltration and changes in cerebrospinal fluid reactions all favor this hypothesis The anti inflammatory and antithermic effect of cortisone accounts for the favorable effect in preventing febrile reactions Another mechanism suggested by the authors is that corticotherapy affects favorably the *concentration of penicillin in the plasma The question is* also raised as to whether cortisone may increase the treponemicidal power of the penicillin

Treatment of Syphilis with Antibiotics Other than Penicillin With growing frequency the physician faces the problem of choosing a therapeutic agent for patients with syphilis who are sensitive to penicillin The choice is between a return to the difficulties and dangers of treatment with arsenic and bismuth and use of some other antibiotic with treponemicidal properties Sidney Olansky (Duke Univ) and Warfield Garson (Univ of North Carolina) reviewed the literature concerned with the treatment of syphilis with antibiotics other than penicillin

Streptomycin was the first of the newer antibiotics to be used but it gained little favor because the large doses necessary to control syphilis were too toxic Chlortetracycline chloramphenicol and possibly oxytetracycline have been successfully used in enough patients to demonstrate their effectiveness in early syphilis benign late cutaneous syphilis neurosyphilis and prenatal syphilis There is little reason to believe that these three antibiotics would not be effective in latent syphilis and cardiovascular syphilis in adequate dosage Carbomycin and erythromycin appear to be prom

(5) A M A Arch Dermat 77 648 650 June 1958

any clinical study and to check on the clinical findings the authors also made measurements on an untempered pressed wood phantom Doses and technics in irradiating the phantom paralleled those used in treating dermatologic patient

With few exceptions some radiation reached the gonadal areas of most patients treated by conventional dermatologic x ray equipment and technics Some of the findings could have been assumed and anticipated especially the doses obtained when irradiating dermatoses near the gonads or when the x ray tube was directed toward the gonadal areas However the fact that radiation reached the gonads despite extensive local shielding relatively large tube to gonad distances and angling the tube away from the gonads was not expected

The total amount of radiation that might reach the gonads of patients during single dermatologic treatments (or in a complete series of treatments) may be higher or lower than the suggested allowable limits (to the population as a whole) of 0 15 r (150 mr)/year depending on the conditions under which radiation is given The dose however is less than the allowable maximum of 0 3 r (300 mr)/week for 13 weeks or an average of 0 1 r (100 mr)/week throughout the year established for the small segment of population occupationally exposed Under exceptional circumstances despite precautionary measures the gonad dose may well exceed either allowable dose

The authors findings point up the need for a critical review and evaluation of indications for and benefits of x ray diagnosis and therapy as well as the need for development and use of improved technics and equipment to reduce x radiation reaching the gonad A joint responsibility for finding ways to reduce the amount of x radiation reaching the gonads during medical x irradiation must be shared by designers and manufacturers of x ray equipment by radiation physicists and by physicians and radiation technicians

Diagnostic and therapeutic units need redesigning to reduce to a minimum the amount of stray and scattered radiation Physicists need to measure stray and scattered radiation to be able to advise on methods and means for reducing the gonad dose Physicians and medical personnel using x radiation should realize that during diagnostic and thera

below the accepted weekly permissible average dose of 100 mr

However, the survey revealed that there was an undue amount of stray radiation when the x ray apparatus was in use Stray radiation in the corridors was high There was no lead lining in the walls The explanation for the low exposure of personnel according to the film badges is that the x ray apparatus was in operation only a few hours every week

The importance of standing well behind the protecting shield of the control booth of the x ray apparatus was emphasized by a reading of 1 000 mr/hour at the entrance to the booth While the x ray machine is running the operator standing at the site of maximum protection inside the control booth is exposed to a significant amount of radiation At this site the maximum permissible average dose of 100 mr/week is reached in slightly over 8 hours

► [We hope that this article will alert all those who administer ionizing radiation in management of diseases of the skin to survey their quarters and make certain that the operators of their equipment are properly and adequately protected against exposure to such radiation It is our opinion that the physician responsible for the administration of such radiation should make known to the physicist entrusted with the calibration of his radiation equipment any questions that he might have concerning radiation protection The responsibility of the physicist today goes beyond measuring the output of the machines and supplying a written report He should also seek and measure any sources of radiation which might act as hazards to the operating personnel Such detailed surveys should be done at the time of the installation of the radiation equipment where this has not been done there is no time like the present —I d]

Studies on Quantity of Radiation Reaching Gonadal Areas during Dermatologic X ray Therapy—II *Methods quantitative measurements and analyses of some important factors influencing gonad dose*—Victor H Witten Marion B Sulzberger and William D Stewart (New York Univ Post Grad Med School and Skin and Cancer Unit) attempted to evaluate the effects of a large variety of factors which could influence the gonad dose of x *radiation The most important* factors are (1) distance from the x ray tube to the gonads (2) tilt of the tube in relation to the gonads (3) position of the patient (4) scattered radiation from various sources and (5) leakage radiation from the tubehead

In an attempt to reduce the number of variables present in

(1) A M A Arch Dermat (483 (93 December 195

A lead cone devised to extend from the x ray tube aperture to the surface being irradiated and to border the field to be irradiated reduced the gonad dose in the seated phantom by 50% The cone decreased the gonad dose by eliminating the peripheral or outer portions of the primary x ray beam These portions of the primary beam appear to produce most of the scatter from the table and to be the source of direct radiation to the gonads of patients seated close to the table Reduction of the size of the irradiated field direct shielding of the gonad area and use of a sandbag for supporting the treated part proved effective in reducing the gonad dose A combination of these technics can reduce this dose 97%

The technics recommended for reducing the gonad dose are all readily available inexpensive relatively speedy and simple cause no discomfort or undue alarm to the patient and are effective in reducing the dose to a level such that the concern now voiced over the possible genetic effects of therapeutic radiation at least as given for most dermatologic disorders may be greatly alleviated

► [Although there are no reports of genetic damage having actually been produced by properly administered dermatologic x ray therapy all possible measures must be taken to reduce the gonad dose to the absolute minimum We have utilized the inexpensive and simple protective technics described in this report with no difficulty Patients occasionally ask what we are wrapping around their midriff and why We tell them frankly that it is a sheet of leaded rubber intended to offer them every protection possible and they seem to accept this explanation without alarm—Eds]

Clinical Evaluation of Radiation Therapy in Psoriasis Leonard C Harber[8] (Rigshosp Copenhagen) compared the effectiveness of conventional x rays and grenz rays in treatment of 76 unselected patients with psoriasis X rays were administered in doses of 160 r once a week using 50 kv 40 ma and 1 mm Al with a half value layer of 0 85 mm Al Grenz rays were given in doses of 200 r once a week using 11 kv 15 ma half value layer 0 022 mm Al and 12 cm distance In each case large patches of psoriasis were divided into three areas one was treated with x rays another with grenz rays and the third was untreated and used as a control If large patches were not available three small discrete patches were used

A marked difference was observed in the improvement of irradiated sites compared with nonirradiated controls Im

(8) A M A Arch Dermat. 77 5 4 538 May 1958

peutic procedures they and their patients may receive x radiation to the gonadal areas Thus every effort should be made to reduce gonad doses to the lowest level consistent with effective use The physician must know the various sources of radiation reaching the gonads and master technics to reduce or eliminate the gonad dose

III Shielding technics and other precautions for reducing gonad dose —Stewart Witten and Sulzberger[8] investigated these technics on the basis of measurements made of the amount of ionizing radiation reaching the gonadal areas of a pressed wood phantom Previous studies showed that the dosimeter readings recorded in the phantom corresponded closely with those recorded by dosimeters placed on the skin as close as feasible to the gonadal area of patients receiving as nearly as possible similar amounts of radiation under similar conditions Measurements were made with Keleket K 112 pocket dosimeters with a recording range of 0 200 mr

A lead rubber sheet 1/16 in thick wrapped around the lower two thirds of the phantom lying horizontally on the x ray table reduced the gonad dose from therapeutic radiation to the upper chest or back by about 50% This indicates that about half the radiation reaching the gonad area of the phantom under shielded conditions apparently is from leakage and external scatter radiation and the other half is in part scatter from the primary beam originating within the phantom itself The gonad dose can be further reduced by using therapeutic radiation of lower kilovoltage Reducing the kilovoltage from 90 to 52 reduced the gonad dose to an average of 20% of the dose recorded in the unshielded phantom irradiated with the higher kilovoltage

The phantom studies imply that when patients are treated in a seated position in a chair adjacent to the x ray table the ovarian area in females may be expected to receive less than half the amount of radiation which will be received by the male gonads Approximately three fourths of the gonad dose in a seated patient originates as scatter from the table and adjacent structures The remaining one fourth comes directly through the x ray tube head as leakage and or from the peripheral portion of the primary beam

(8) J Inv st Dermat 30 237 247 May 58

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(9) A M A A h Derm t 77 554 558 M y 19 8

provement was less marked in large patches with large flaking scale and lichenification than in large patches with micaceous scale and less prominent lichenification or small discrete patches In over 70% of the studies there was no significant difference in the degrees of improvement produced by the two types of irradiation Improvement was discernible in about 50% of cases after only one treatment but the greatest improvement in irradiated sites occurred after two or three weekly treatments

When improvement occurred in the control it was uniform throughout the entire area, the portion of the control nearest the irradiated site did not improve more than the central area This fact plus the striking difference in improvement noted between irradiated and nonirradiated areas strongly reinforces the concept that irradiation produces improvement through direct cellular action rather than by release of a humoral substance

► [This study once more confirms that grenz rays (half value layer 0 022 mm Al) are as effective as x rays (half value layer 0 85 mm Al) in causing involution of psoriatic patches It does not provide data on the duration of the improvement In our clinical experience the beneficial effect of x rays is longer lasting in psoriasis than that of grenz rays However this difference in effectiveness is amply compensated for by the fact that grenz ray treatments to individual areas can be repeated with infinitely greater safety than x ray treatment thus the patient can derive the benefits of repeated courses of grenz ray therapy over the years —Eds]

***Investigations on Optimal Dosage in Treatment of Skin* Carcinoma** are reported by M K Polano[1] (The Hague) Introduction of reliable dosimeters and x ray tubes with beryllium windows has made it possible to develop technics of irradiation of skin malignancies which limit the dosage largely to the diseased tissue Penetration of x ray energy beyond the skin tumor was limited by Plaats by bringing the focus as near as possible to the skin and by using radiation generated at 50 kv by a tube with a window with a filter equivalent of 0 2 mm Al His method proved excellent for treatment of skin carcinomas except for the obvious drawback that because of the short skin focus distance the field that can be exposed to a homogeneous surface dose has only a small diameter

The author found that by using 25 kv 0 2 mm Al filter half value layer 0 1 mm Al and a focus skin distance of

(1) J belge radiol 41 3 58 1958

n he could obtain a depth dose almost identical with of the Plants apparatus u ed at 2 cm focus skin distance using the same kilovoltage without filter and a half value r 0 043 mm Al an even greater percentage of the radia energy could be confined to the first few millimeters of ue The chief advantages of this technic are the enhanced ty factor and excellent cosmetic results

measurement of the depth of skin carcinomas and pre cerous lesions in 207 biopsy specimens most skin cancers le keratoses and lesions of Bowen s disease were found e less than 3 mm thick About one third of the carcinomas all the precancerous lesions were less than 2 mm thick reating such lesions the dose should be adjusted as ac ately as possible to the actual thickness of malignant tis

The author treated 102 cutaneous carcinomas using a th dose of 3 000 r In the original article a table is given wing surface doses which may be u ed to obtain 3 000 r various depths To avoid unnecessary complications in st cases 25 kv unfiltered was used for irradiation up to nm depth and 25 kv with 0 2 mm Al filter for deeper adiation Usually the total dose was given in 1 session e dose was fractionated only in tumors more than 3 mm ck of great diameter or lying just over bone or cartilage After such treatment there were primary recurrences in 8 the 102 carcinomas A 5 year primary cure rate of 78% was tained This rate actually gives an unfavorable impression the results because with this method of treatment recur nces are easily re treated without danger of sequelae In e present group all recurrences except 2 in which surgery is indicated were re irradiated and the patients have re ained symptom free The recurrences originated in the argin of the irradiated field and apparently were due to radiation of too narrow a margin of apparently healthy sue around the tumor or to multicentric origin of the tu or All lesions that recurred were basal cell carcinomas

[In this study an attempt is made to correlate the quality of radiation ed with the histologically established approximate thickness of the le ns Th s is in keeping with the principle that quality and dose of radia on should be selected so as to destroy the skin cancer without extensive amage to the surround ng and underlying structures The question wheth r the h gh rate of failures was actually due to the reasons given by the uthor remains unanswered.

We are staunch advocates of applying the principle of using a selected quality and dose of radiation in the *management of benign skin lesions* also In this way the undesirable effects of irradiation can be avoided and safety will become a word with meaning —Eds]

Treatment of Carcinoma of Alae Nasi by Fractional Doses of X rays is advocated by Norman M Wrong[2] (Univ of Toronto) because this method produces a good cosmetic result with a *minimum of undesirable sequelae and a low recurrence rate*

METHOD —A total dose of 3 500-4 200 r was given depending on *the size of the lesion* This was divided into 6 or 8 equal doses given daily At the first visit a biopsy specimen was taken, and if necessary the growth was flattened to skin level by electrodesiccation A small plug of *gauze impregnated with zinc ointment was inserted into the* nostril to protect the septum when the roentgen treatments were given

The quality of radiation used in treatment of basal cell carcinoma of the alae nasi is important and the softer the x ray used the better the effect as most of the rays would be absorbed in the ala In the present series factors were *70 kv 5 ma* target skin distance 4½ in no added filter half value layer 0 77 mm Al

The alae nasi appear to be particularly prone to basal cell carcinoma Of 112 consecutive skin malignancies *27* involved the alae nasi and all were basal cell carcinomas None of the *27* lesions recurred after treatment with fractional doses of x ray *Follow up* has been *6* months to 5 years Larger lesions have been replaced by white depigmented scars, but none has shown any pronounced telangiectasia In no case has there been persistent soreness of the nose after treatment

► [The methods and total dosages described by the author are similar to those used by many dermatologists in the United States and Canada They generally produce excellent therapeutic and cosmetic results Of course there is a lower limit to the softness of the radiation which may be used We usually *administer treatment at intervals of 2 days* rather than daily although the total dose (ordinarily greater than 4000 r) is given in essentially the same period of time —Eds]

Treatment of Myxomatous Cutaneous Cysts (synovial lesions of the skin) is discussed by *Robert B Engle*[3] *(Univ of* Southern California) The cause of these cysts is believed to be a focal degeneration of the corium Whether this results from local trauma a small arterial thrombosis or some other factor is not known The first change is a degeneration or resorption of the collagen *in a localized area leaving fibro*

(2) A M A Arch Dermat 77 73 8 Jan 1958
(3) Radiology 71 93 35 July 1958

blasts with but little intercellular material Basophilic mucoid material collects between the fibroblasts and they gradually disintegrate creating multiple minute cavities which coalesce to form a gross cyst containing clear glairy gelatinous or syrupy fluid This fluid is not secretory but arises from degeneration of local connective tissue The inner wall of the cyst is irregular at first Later it becomes smoother and denser There is no epithelial or endothelial lining No communication exists with subjacent structures such as tendons joints or bursae

Myxomatous cutaneous cysts treated by incision and drainage curettage cauterization fulguration freezing with carbon dioxide snow and surgical excision invariably recur In general radiation therapy is indicated The author describes 4 patients treated with x rays Two cysts failed to respond to doses of 1 000 r superficial x irradiation (100 kv 3 2 mm Al 25 cm target skin distance One cyst showed a partial response (satisfactory to the patient) to a single dose of 2 000 r The fourth cyst responded to 1 400 r of more penetrating radiation (half value layer 1 2 mm Cu) Further studies of the optimal quality and quantity of radiation for these lesions are indicated

► [We have had satisfactory results with fractional x ray therapy of some synovial cysts However a seemingly more logical form of treatment, that of injecting hyaluronidase was suggested by Gotz and Koch (Arch klin u exper Dermat 204 361 1957) —Eds]

Results of Chaoul s Method of X ray Treatment (Contact Therapy) in Skin Cancer Branislav Gadjanski[4] (Univ of Belgrade) reports on the 3 year results in 450 patients who had x ray contact therapy for skin cancer In all but 25 the cancer was localized in the face There was no sex predilection Basal and prickle cell cancers had about the same incidence Papillomas especially those of the lip were considered malignant tumors some metastasized later

Of 339 patients available for the first follow up examination about 1 3 months after treatment completion 74% were symptom free After 3 years 41 5% were asymptomatic 13 7 were improved and in 3 5% treatment failed The death rate was 6% but only 1 55% died of their skin condition No follow up studies were available in 47 5% of the patients Necrosis was encountered mostly in elderly thin patients

(4) Rad i a straza 9 297 301 1957

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Treatment of Carcinoma of Alae Nasi by Fractional Doses of X rays is advocated by Norman M Wrong[2] (Univ of Toronto) because this method produces a good cosmetic result with a minimum of undesirable sequelae and a low recurrence rate

METHOD —A total dose of 3 500-4 200 r was given, depending on the size of the lesion. This was divided into 6 or 8 equal doses given daily At the first visit a biopsy specimen was taken and if necessary the growth was flattened to skin level by electrodesiccation A small plug of gauze impregnated with zinc ointment was inserted into the nostril to protect the septum when the roentgen treatments were given

The quality of radiation used in treatment of basal cell carcinoma of the alae nasi is important and the softer the x ray used the better the effect, as most of the rays would be absorbed in the ala In the present series factors were 70 kv 5 ma target skin distance 4½ in no added filter half value layer 0 77 mm Al

The alae nasi appear to be particularly prone to basal cell carcinoma Of 112 consecutive skin malignancies 27 involved the alae nasi and all were basal cell carcinoma None of the 27 lesions recurred after treatment with fractional doses of x ray Follow up has been 6 months to 5 years Larger lesions have been replaced by white depigmented scars but none has shown any pronounced telangiectasia In no case has there been persistent soreness of the nose after treatment

► [The methods and total dosages described by the author are similar to those used by many dermatologists in the United States and Canada They generally produce excellent therapeutic and cosmetic results Of course there is a lower limit to the softness of the radiation which may be used We usually administer treatment at intervals of 2 days rather than daily although the total dose (ordinarily greater than 4000 r) is given in essentially the same period of time —Eds]

Treatment of Myxomatous Cutaneous Cysts (synovial lesions of the skin) is discussed by Robert B Engle[3] (Univ of Southern California) The cause of these cysts is believed to be a focal degeneration of the corium Whether this results from local trauma a small arterial thrombosis or some other factor is not known The first change is a degeneration or resorption of the collagen in a localized area leaving fibro

(2) A M A Arch Dermat 77 73 8 January 1958
(3) Radiology 71 93 95 July 1958

the u efulness to heman,ıomas that are not over 2 3 mm thick

In the first treatment series total do e of 3000 rep was given divided into single doses of 1000 rep each 1 week ipart After 6 week the le ion was re evaluated If suffi cient regression had not occurred another 1000 rep was delivered Follow up examinations were one every 6 weeks and when necessary 1000 rep was repeated each time until over all dose of 6000 rep was reached

After the second or third sitting the hemangiomas usually changed from bluish red to a lighter red and its surface be came smooth If healthy skin was included in the radiation area ome erythema appeared there About 6 weeks after the first treatment series previously elevated hemangiomas had regres ed to skin level Occasionally a pigmented area ap peared around the radiation site

► [Sr is a good ource for pure beta ra liation When prepared in the form f well constructed plaques it is safe to use as a surface applicator Gr t care must be taken however to make certain that there are no leak from the irrad ating source since Sr^{90} localizes in bone and i a danger ou compou d when ab orbed via the mouth or other routes —E ls]

Hemangiomas Treated and Untreated George C An drew Anthony N Domonkos Victor M Torres Rodriguez and John K Bembenista[6] (Columbia Univ Presbyterian Med Center) studied the records of 1 113 patients (710 fe male) with va cular nevi Of these 329 had hemangioma implex (trawberry mark) and 584 had hemangioma caver nous um Of 153 patient with hemangioma simplex who re ceived no treatment 102 were observed adequately In 64 (63) the lesion involuted or improved within 5 years wherea in 38 (37) the hemangiomas persisted In patients who had hemangioma implex with spontaneou involution 83 of the lesion were 1 cm or le s in diameter It may be concluded that any hemangioma implex on the face measur ing 1 cm or more should be treated without delay because tho e of larger ize have poor pos ibilities of involution without therapy Occa ionally a large hemangioma disap pear pontaneou ly without car but other have been noted t per i t grow ulcerate and become a serious problem Be cau e the co metic appearance of the site i u ually the most important con ideration early institution of treatment and

J A M A 165 1114 111 N 19

especially when the skin in the treatment area was atrophic or tightly stretched over the underlying bone such as on the ridge of the nose over the zygoma or in the corner of the eye

The author did not use very large radiation fields because the peripheral areas of large lesions do not get enough radiation if one field is used This may lead to peripheral recurrences

TECHNIC—The Siemens Monopan machine was used and almost always an oblique electrode was applied Average total dose was 6 000 r divided into daily doses of 500 600 r To prevent necroses fixed fields were avoided and moving fields were used Radiation was given until the lesion eroded causing the tumor to melt away Gratifying cosmetic results were achieved by covering the treatment area with a thin sheet of cellophane which prevented development of brown pigment rings around the smooth scar

Chaoul s treatment method should not be applied to patients who previously had x ray radium surgical or coagulation therapy because these methods lead to unphysiologic conditions in the stroma with subsequent severe circulatory disturbances that hinder reparative processes

Strontium 90 Dermaplates and Their Use in Treatment of Hemangiomas were studied by R Gersing (Bonn Germany) Among the beta radiating isotopes suitable for superficial treatment Sr^{90} is especially favored because it has a long half life (25 years) and is available in sufficient amounts Sr^{90} decays into Yt^{90} which has a half life of 61 hours and transforms into stable Zr^{90} Sr^{90} and its decay products are pure beta emitters In closed carriers as used in therapeutic applicators the two isotopes are in radioactive equilibrium The dermaplates are cylinders made of nickel the hollow part of which contains the radioactive substance The window of the cylinder is 0 1 mm thick and permeable to beta radiation whereas the top is 1 5 mm thick and impermeable to radiation The diameter of the commercially available cylinders is 9 9 16 5 or 23 mm The two dermaplates used by the author had radiation activity of 20 mc /4 sq cm and 100 mc /2 sq cm respectively

The limited penetration of Sr^{90} makes it possible to treat hemangiomas over radiation sensitive areas such as growth zones of bones near the breast gland and over the eyes (lid hemangiomas) The steep decline of the isodose curve limits

(5) Fortschr Geb Rontgenstrahlen 88 33 41 Feb 1958

not have recovered completely from the damage resulting from the first series of treatments If a third or fourth course of treatment is given symptoms of overexposure may appear When radiations with a half value layer of 2 mm Al or more are used the danger point is reached even sooner

When electrons from high voltage generators are used for irradiation the total body dose is considerably below that produced by x rays With 2 5 Mev electrons for application of 300 r to the skin the average dose to the body is 67 r with 1 5 Mev electrons the average total body dose is 36 r With electrons therefore it should be possible to treat cutaneous lesions with a higher dose and to treat recurrences more often with fewer symptoms of radiation damage to the body

In the treatment of extensive dermatoses if monoenergetic electrons cannot be used it is advisable to use x rays with a half value layer between 0 5 and 1 mm Al An effort should be made to shield any part of the skin not involved to reduce the total dose delivered to the body

► [This article points out one of the very important aspects to be considered when using ionizing radiation in the treatment of diseases of the skin Furthermore it clearly demonstrates that here too it is advisable to use the softest effective radiation feasible in treating benign dermatoses —Eds]

Telepanirradiation of Generalized Dermatoses with Beryllium Window Tubes Dose Rate in Depth Uniformity of Field and Illumination Gian Luca Sannazzari and Giuseppe Lovera[8] (Univ of Turin) report that the introduction of apparatus with beryllium window tubes has created new and better technical possibilities in dermatologic x radiation because it is now possible to deliver rays at a wavelength greater than ever before (those generated by energy of 15 50 kv) With these tubes at standard focus skin distances (20 30 cm) the field of radiation can be large the rays reaching the body are practically entirely absorbed within the skin and the duration of each sitting is brief With a filter variations in half value layer can be obtained making possible a true cutaneous stratitherapy

The energy filter combinations preset in four switches are switch 1 10 kv without filter switch 2 29 kv 0 3 mm Al switch 3 43 kv 0 6 mm Al and switch 4 50 kv 1 mm Al

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[8] Dermatologica 115 48 6 November 1957

prevention of secondary infection are recommended The likelihood of ulceration of hemangiomas on the lips nostril eyelids and ears suggests that these lesions should be treated even though they are less than 1 cm in diameter

Of 135 patients with hemangioma cavernosum who received no treatment during the first 5 years of life and who could be followed adequately, 22 (16%) showed involution or improvement of the lesions during the 5 years The high percentage of persistence in untreated cavernous hemangiomas indicates the desirability of treatment for all cavernous hemangiomas

The method of treatment should be carefully chosen to secure the best cosmetic results The authors feel that radium therapy properly administered, assures excellent results without risk of radiation sequelae In some patients surgical excision ligation, solid carbon dioxide or roentgen ray treatment is indicated

► [Some other authors have reported a much higher incidence of spontaneous cures Regardless of the particular school of thought with which one agrees it is the responsibility of the physician to advise the patient or his family whether therapy is required and if so to select the method of therapy best suited for managing the particular lesion In instances in which treatment is considered unnecessary it is best to see the lesion at appropriate intervals in order to follow it course and institute active therapy if necessary —Eds]

Superficial Radiation Therapy of Large Skin Areas R Braams[7] (State Univ of Utrecht) calls attention to the relatively large doses of x rays that are delivered to the total body when extensive skin lesions are treated Experiments on monkeys have shown that a total body dose of 450 500 r x radiation delivered in a relatively short time (a few weeks) has a 50% chance of causing a lethal effect A total body dose of 450 r means that in the course of irradiation each part of the body received about 450 r The human 50% lethal dose is believed to be about the same as that for monkeys

Braams presents a method for calculating the approximate *total* body dose after extensive irradiation of the skin surface An average dose of 225 250 r is given to the whole body when the average patient receives 300 r (3 doses of 100 r each) with a half value layer of 1 mm Al to the total skin surface If such treatment is repeated in a year or less because of recurrence of the dermatosis it is probable that the body will

(7) Dermatologica 117 204 214 October 1958

by soft x rays it is possible to deliver super oft x rays The e new tubes thu allow irradiation only of the most su perficial layers of the skin (epidermis and papillary bodies) or of deeper layer as the need may arise

Brown reviewed statistically the therapeutic results in 773 patient treated for eczema with x rays Considerably better results were obtained with lower doses (60 r) and weak radi ation (tube with beryllium window 30 kv 0 5 mm Al and tubes with 0 3 mm gla s walls 70 kv without filter) than with higher doses (100 r) and stronger radiation (tube with glass wall 100 kv 1 2 mm Al)

Even in acute eczema in which x ray treatment was for merly thought inadvi able good results were achieved by reducing the dose to 10-15 r

► [We al o are in favor of carefully selecting the particular quality of radiation be t suited to treat the particular skin disease with the thought t delivering the radiation as much as possible within the involved portions of the skin As most benign d rmatoses are limited within the uppermost 1 mm of t ssue it is logical to use radiation softer than that conventionally applied in dermatologic therapy i e half value layer of 0 8-1 0 mm Al Grenz radiation with half value layer of 0 018-0 036 mm Al is ideally suited for treatment of many of these dermatoses At times somewhat harder radiation with half value layer of 0 5 mm Al may be used Knowl edge of the depth-dose curve for the various qualities of radiation will be f distinct help in deciding on the most suitable type of radiation to use —F is]

Radiation Damage Caused by Shoe Fitting Fluoroscope

H Kopp[1] (Finsen Inst Copenhagen) report a case

Woman 56 had a typical radiodermatiti of the dorsal surface of th right toes with cicatricial changes keratotic scaling depigmenta ti n telangiecta ia and ulceration She allegedly had never had radi ati n treatment or x ray examination She had however worked for 10 year in a hoe hop where two shoe fitting fluoroscopes were u ed

Examination of th machines revealed that in one the beam in ten ity at the foot plate wa 2 r/minute and in the other 13 2 r minute A defective lead creen in one fluoro cope expo ed the shop a t nt to trong diffu e radiation while he operated the machine fr m the front part of the foot plate an unscreened cone of ray pa ed in the direction f the cu tomer s abdomen delivering 1 r/min ut in a dult and con iderably more in children

The patient radiodermatitis had apparently re ulted from ex p ur f the foot while dem n trating the fluoroscope to apprehen ive children while trying new hoe model under tran illumination and while upporting the right foot on the platform in front of the foot pen ng while examining cu tomers feet

1 Bri M J 2 13 4 1 4 Dec 195

Some values were measured with the phantom chamber for soft rays and Siemens universal dosimeter The rate of distribution in depth along the central ray was at a distance *of 1 m half the dose with switches 2, 3 and 4 at 5 5 12* and 18 mm respectively and at a distance of 2 m half the dose with the switches at 7 5 17 and 26 5 mm The depth at which 70% of the dose was delivered along a line perpendicular to the axis of the tube while moving away from the center of the field was at a distance of 1 m with switches 2 3 and 4 *39 44 and 48 cm from the center and at a distance of 2 m* 53 77 and 87 cm from the center The intensity of radiation at a distance of 1 m with switches 2 3 and 4 was 7 5 97 and 9 1 r/minute and at a distance of 2 m, 1 5 2 6 and 2 5 r/minute

These results indicate that beryllium window tubes are *valuable tools for total body irradiation at a distance for gen*eralized dermatoses

► [After the article by Schurren (J Invest. Dermat 24 463 1955) on teleroentgen therapy with soft radiation from beryllium window tubes a special x ray unit installed by the Picker X ray Company has been used for similar therapy at the New York Skin and Cancer Unit It operates at 50 kv 25 ma with a half value layer of 0 2 mm Al at a distance of 2 m *In our limited experience with this modality it has proved beneficial in some cases of widespread eruptions —Eds]*

Comparative Statistical Studies on Influence of Hardness of Radiation and Size of Dose on Results of X ray Treatment of Eczema were conducted by Roy Hershel Brown[9] (Univ Skin Clinic Zurich) There has been growing tendency to economize with the therapeutic effects of x rays In treatments in which cumulative effects have to be expected exceeding the dose needed for therapeutic effects is a mistake This is true especially for treatment of inflammatory changes as opposed to treatment of neoplasms In the latter possible severe tissue damage can be overlooked for the sake of cure but in the former even relatively slight damage may be considered a failure Because inflammatory diseases involve only a few millimeters of superficial skin tissues it is senseless to apply rays that penetrate many centimeters into the body and exert superfluous or even harmful effects

Superficial x ray treatment has become possible by recently developed x ray tubes that operate on 6 50 or 6 100 kv Due to a beryllium window which can be easily penetrated

(9) Dermatologica 117 215 222 October 1958

membranes and consists of irregular slowly expanding spots of gray brown to blue black Coloration is uneven Tumorous transformation usually takes place late at one or several sites Recognition of these spots is important because they regress well under x ray therapy A third group of melanomas develops spontaneously on previously normal skin Melanomas are usually dark bluish black Occasionally they may be poor in pigment or even unpigmented These may lead to serious misdiagnoses especially when pigment is completely absent (amelanotic melanoma)

Early recognition of a melanoma is important If diagnosis is doubtful it should not be confirmed by biopsy because of possible traumatic spread Rather the tumor should be treated as if its malignancy were proved The lesion should be destroyed by coagulation or excision far into the healthy area Lately the authors have administered x radiation once about 3 000 r followed immediately by excision Even when the regional lymph nodes appear uninvolved prognosis will be improved by their removal Irradiation of involved lymph nodes is advisable before their removal If there are cutaneous and subcutaneous metastases around the tumor only a very wide deep excision (including the fascia) may be successful If the tumor and the metastases involve an extremity amputation may be necessary Metastases to internal organs denote extremely poor prognosis

The author reviewed therapeutic results after 5 years in 104 melanomas At time of treatment 70 of these had no metastases (stage I) 30 showed regional metastases (stage II) whereas 4 had metastases to internal organs (stage III) After 5 years 61% of the patients in stage I were free from symptoms 11 5% in stage II and none in stage III Best results were achieved with melanomas of the head Primary melanomas were not resistant to radiation treatment

With competent treatment neither the surgical nor the x ray method can be said to be superior

► [As in previous years Miescher continues to advocate the use of x radiation as a part of the management of malignant melanomas As pointed out in this article he actually feels that x ray therapy is equal to surgical therapy provided it is done in a competent manner —Eds]

Malignant Melanoma Combined Surgical and Radiotherapeutic Approach Robert J Dickson[3] (Johns Hopkins

[3] Am J Roentgen 1 79 1063 1070 J 1958

Besides the hazard of radiodermatitis from use of sho fitting fluoroscopes the author calls attention to the hazar of increased gonad radiation The dose of radiation to th customer s abdomen during a typical foot examination wi the machines *investigated would be greater than that fro* even large radiologic units In assessing the genetic hazard only irradiation of fertile persons is to be considered Th adds to the difference, because shoe fitting fluoroscopes ar used chiefly for *child* customers, whereas x ray examination are made more frequently in older persons

► [It is unbelievable that the u e of shoe fitting fluoroscopes still is pe mitted in some states and countries As indicated in Kopp s study ther *was not only radiation exposure of the customer s feet but also* of th gonadal and other areas not to speak of the exposures received by th sales personnel routinely using the machines —Eds]

Treatment of Melanomas is described by G Miescher an A Hunziker[2] (Univ Skin Clinic, Zurich) Successful treat ment of malignant tumors depends on early recognition This criterion is generally not difficult to fulfil in skin tu mors and thus the cure rates become practically 100% in *basal cell and prickle cell epitheliomas of small or moderat* size Malignant melanomas however are an exception They have a strong tendency to metastasize due to their charac teristic cells which grow by infiltration and also due to their close *relation to the lymph* vessels and *blood* vessels The tumors spread *through* the lymphatics and through the blood stream Metastases may appear very early while the tumor is only of pinhead size and involve all organs or only after 10 20 years which would indicate that melanoma cells may remain dormant in various tissues

Melanomas often start from a pigmented nevus There seem *to* be no nevus types predisposing to malignancy Characteristics that point to malignant transformation of a nevus are sudden increase in growth usually accompanied by increasing pigmentation signs of inflammation bleeding or crust formation and itching Darkening *of the nevus* with out increase in size and without inflammation does not in dicate malignancy

Malignant melanomas may develop from melanotic pre cancerous area This form of precancerous state *is common* est in the face and on the hands, occasionally on the mucous

(2) Schweiz med Wchnschr 88 03 09 Mar 1 1958

was no statistical difference between results of local therapy and those of wide surgical excision but the groups were fairly small In a comparison of patients treated surgically and those in whom radiation therapy was used there was considerable improvement with the addition of radiation therapy However the difference in survival rates was just statistically significant and these figures cannot be advanced as definite proof of the advantage of giving radiation therapy to these patients On the other hand the patients in the different groups were probably not strictly comparable First the patients treated by surgery alone were probably in a relatively earlier stage of the disease Second many patients with more advanced cases were treated by irradiation and were included in that group These considerations lend force to the suggestion that postoperative and palliative radiation therapy tends to improve the prognosis in malignant melanoma

The natural history of malignant melanoma is variable and even in apparently advanced cases long term survival is frequent The present series may include a high proportion of such cases or there may have been a relatively large number of patients with early stage of the disease Attempts were made therefore to compare this series with others from the literature in regard to age sex body distribution and staging and it would appear that there is a fair degree of similarity The 5 year results of wide surgical excision alone were comparable with others reported in the literature but when radiation therapy in adequate dosage was given a higher survival rate was obtained When the material is broken down into stages the number of patients who survived more than 5 years in stage I and II is increased (stage I 0% stage II 21.6%) Prognosis in stage III is still negligible

Though the evaluation of any treatment method is difficult in such an unpredictable disease the improvement in survival rate over that reported by other authors totaling nearly 2 500 cases indicates a substantially beneficial effect from postoperative and palliative radiation therapy The opinion that radiation therapy is valueless in malignant melanoma is probably based on experience with inadequate dosage

► [It is gratifying to see that the management of melanoma is being re

Hosp) describes results of treatment of 234 patients with malignant melanoma seen at Toronto General Hospital Johns Hopkins Hospital and the USPHS Hospital Baltimore There were 102 patients (43 5%) in stage I (localized melanoma confined to skin including local recurrences and nearby deposits in cutaneous lymphatics) 93 patients (39 3%) in stage II (with regional lymph node metastases confined to one node station only) and 39 patients (16 7%) in stage III (with metastatic involvement of two or more groups of nodes or distant metastases)

The treatment policy at Toronto General Hospital was to operate on all patients in stages I II and occasionally III with wide excision of the primary tumor and the immediate lymph drainage areas and then to give postoperative radiation therapy to all areas found on histologic examination to contain disease Not infrequently however only surgery was used A few patients at the two Baltimore hospital were treated by surgery with irradiation but most received no radiation therapy except as palliative treatment of recurrences

Radium and roentgen rays were used with almost equal frequency Teleradium therapy both to primary and metastatic sites was given to several patients the dosage varying between 4,800 and 6 500 r in 4 6 weeks Those receiving roentgen therapy were usually given 100 kv radiation to a dose of 5 000 r in 10 days to the primary area with an estimated tumor dose of 4 000 5 000 r to lymph node bearing areas at either 200 or 400 kv in about 5 weeks

In 71 patients initial treatment consisted in application of caustic solutions or local surgical removal without any further treatment within a 1 month period 42 were treated by definitive surgery and the other 121 received radiation therapy immediately after the initial surgical intervention In many patients the surgery was local and many stage III patients were included in the group receiving radiation therapy

Of the 121 patients in whom radiation therapy was used 41% survived 5 years About one fourth of those treated by excisional surgery without irradiation lived 5 year and about one fifth of those having only local therapy during the 1st month of treatment were still alive for this period There

at 3 minutes and Mexicans or Sicilians at 5 minutes Subsequent exposures as tolerance develops rarely exceed 12 minute except for Mexicans Several thousand treatments have been given in the ultraviolet cabinet and patient acceptance has been excellent Pityriasis rosea psoriasis atopic eczema neurodermatitis and other generalized dermatoses have continued to respond at least as well as to cold or hot quartz therapy

The ultraviolet cabinet has several advantages Irradiation of the entire body requires about one fifth of the time needed with other technics No warm up period is necessary for the lamps and no cooling off period is required before reuse Heat production is minimal the lamps can be touched at any time without discomfort Because the tubes are lateral to the patient there is no chance of spontaneous or induced breakage leaking hot mercury by gravity on a patient below the light source with resultant thermal burn Ultraviolet coverage of the entire skin surface is more uniform than with standard technics Installation operation and maintenance are easy and economical

The only untoward incident in 4 years operation occurred when a patient who had many exposures previously removed the goggles and read by the light of the 8 lamps for a 12 minute exposure A mild keratoconjunctivitis resulted

D Surgical Therapy

Indications for Abrasive Therapy are described by E H Hermans Sr and E H Hermans Jr (Rotterdam) Generally any skin abnormality that is due to a disease congenital malformation or accident can be considered for abrasive therapy independently of its size Abrasive therapy should not be tried on persons who have a tendency to extensive keloid formations or in skin diseases that are not yet quiescent The more disturbing the cosmetic changes the better will be the results of abrasive therapy

Indications for abrasive therapy are grouped according to the degree of difficulty involved in handling them (1) lesions which protrude from the skin such as fibromatous or verrucoid nevi hyperkeratoses rhinophyma etc —the least

(5) H tarzt 9 3 4 3 6 August 1958

evaluated and revised There is much evidence that malignant melanomas are not as radioresistant as some of the vociferous advocates of exclusive use of surgery (and sometimes of extremely radical surgery at that) would have us believe

Miescher (A M A Arch Dermat 200 215 1955) pointed out years ago that the supposed radioresistance of malignant melanoma should not prevent one from using radiation therapy for these lesions (see also preceding article) Jørgsholm and Engdahl (Acta radiol 44 417 1955) reported surprisingly good results from radiotherapy alone Evidence such as this is accumulating and we sincerely hope that the near future will bring cooperative efforts between dermatologists surgeons and radiologists in the attempt to improve the favorable results in the management of this frequently fatal tumor —Eds]

Ultraviolet Light Therapy Utilization of Tubular Fluorescent Lamps in Cabinet for Generalized Simultaneous Irradiation is described by Murray C Zimmerman[4] (Univ of Southern California) The ultraviolet source is 8 Westinghouse fluorescent sun lamps 48 in long 40 watt FS40T12 Two of these lamps fit into each of four standard bipin double socket 48 in fluorescent fixtures The cabinet is 3½ × 2½ ft set in a 5½ × 6 ft dressing room A fluorescent fixture with 2 lamps is set vertically at each corner The tubes are turned on by a 15 minute automatic electric timer switch similar to the x ray timer The patient is observed through an ultraviolet opaque window The surrounding dressing room is convenient but not necessary The cabinet arrangement can be used in any closet bigger than 2½ ft square or in a 2½ ft corner of the treatment room

TECHNIC —The patient is escorted into the dressing room told to disrobe completely except for shoes and socks then to knock on the outside door for the nurse As the nurse enters the dressing room the patient steps into the ultraviolet cabinet and shuts the door Skolex Sunscreen cream is smeared thinly on the nipples of all patients and on the glans of circumcised males The patient wears protective goggles or if there are no facial lesions a towel may be wrapped around the head and held with the hands locked behind the neck The nurse turns on the timer then sets a second separate spring timer to ring a bell at the same time as the built in timer shuts off the lights The patient is told to leave the cabinet and dress when the bell rings or the ultraviolet lights go out During treatment the patient stands in the center of the cabinet facing the rear wall with the feet slightly apart He stands still or alternately raises the knees to expose the medial thighs if these are involved

The light source has a continuous ultraviolet spectrum 90% between 2 800 and 3 100 A Thin skinned blondes or redheads are started at 1 minute exposures dark brunette

(4) A M A Arch Dermat 78 646 652 Nov ember 1958

thi method of treatment were skeptical about its usefulness for precancerous conditions

Of 33 correspondents with experience in the use of dermabrasion for actinic or senile skin 30 were enthusiastic or satisfied with results obtained Over 1 300 patients have been treated by this group Protection is relative rather than absolute since some new keratoses or epitheliomas develop in planed areas However recurrences are much less frequent than in adjacent unplaned skin or before performance of the prophylactic procedure

Some dermatologists have used planing to remove single keratoses Though this is a successful method Ringrose in unpublished work has shown that freezing with dichloro tetrafluoroethane (Freon 114) removes the keratoses as well a does freezing followed by planing If further investigation confirms this observation then dermabrasion is indicated in the treatment of premalignant skin only as a prophylactic measure since simple freezing is much easier on the patient than planing

Chronic radiodermatitis was planed by 22 dermatologists with experience in 101 cases Eleven who reported found the procedure satisfactory 3 fair and 8 poor or unsatisfactory Most of the criticism revolved around scarring and slow healing The author points out that chronic radiodermatitis is more than a cosmetic defect so results in this condition should not be judged by the standards applied to treatment of acne scars Eradication of the tendency toward malignant degeneration is the aim of treatment The time required for healing is of no great importance Surgical excision and skin grafting are the only other possible treatments in extensive ca e of radiodermatiti The morbidity and co t are much greater with uch procedures than with planing and the metic result are often no better

Evaluation of the treatment of leukoplakia by planing is impo ible at thi time because of lack of extensive experience but the approach i feasible promi ing and nonscarring Recurrences are the rule in xeroderma pigmentosum becau e the ba ic genetic weakne s is not removed Results in epithelioma adenoide cysticum appear promising Good re ults in 1 patient with arsenical kerato e were reported

Some dermatologi ts reported excellent results in the

difficult to treat (2) scars level with the skin surface such after cut wounds operations plastic surgery etc (3) dimpled scars which can be treated satisfactorily if not too deep, (4) deep scars such as in infiltrative forms of acne after herpes zoster smallpox etc if not too large and atrophic, (5) color changes in the skin surface due to rosacea tattooing flat pigment nevi vascular nevi etc

Results of abrasive therapy besides depending on the type of skin changes depend also on the patient's age localization of the skin changes and the type of skin Thick skin with many appendages usually is more amenable to treatment than thin skin The older the patient the thinner and more atrophied is the skin and the poorer is its regenerative ability Very young persons also have extremely thin skin After puberty the skin is usually more suitable for treatment The extensor surface of the extremities the back and the neck have a thicker skin than do the flexor surfaces or the abdomen The skin of the eyelids and at the angles of the mouth is extremely thin Persons with a dark complexion usually have thicker skin with more appendages than do fair skinned persons

► [In every patient physical *and* psychologic findings (over all attitude and acceptance of their acne and their acne scarring) must be considered before decision is made as to whether to carry out dermabrasion in acne scarring Furthermore the patient should be carefully instructed regarding the degree of improvement that can be anticipated All who have had experience with this technic certainly have encountered an occasional patient who is not satisfied with what has been accomplished regardless of how worth while and more frequently patients who are overenthusiastic about the results achieved

In the abstracts that follow Epstein and Ayres *et al* advocate use of dermabrasion in actinic and senile skin showing changes of atrophy telangiectasia and keratoses as the best method of treatment for this particular precancerous condition —Ed]

Planing for Precancerous Skin Follow up Study is reported by Ervin Epstein[8] (Highland Alameda County Hosp Oakland Calif) A questionnaire was sent to 120 dermatologists known to use planing in their practices Answers from 103 indicated that there is relatively little disagreement among those with experience in the use of dermabrasion for precancerous skin Most feel that planing is a promising treatment especially for prevention of recurrences However many dermatologists who have not used

(8) A M A Arch Derm t 7 6 6 681 J ne 19 8

Planing provides a nonscarring method for treatment of keratoses as well as a prophylaxis against skin cancer by replacing the sun damaged precancerous epidermis with new epidermal cells derived from the cutaneous adnexa Five depths of planing can be delineated during the planing procedure (1) first the pigment vanishes indicating that the major portion of the basal cell layer has been removed (2) myriad of yellowish macules less than 0 5 mm in diameter indicate that the upper dermis has been reached making the pilosebaceous apparatus visible (3) as planing goes deeper the surface appears studded with yellowish lobulated papules which are the sebaceous glands that have been cut across and is the depth usually achieved in moderately deep planing (4) if planing is carried deeper decided resistance of the tissues is encountered primarily because the tissue is below the penetration of freezing (about 2 mm) If freezing is done again at this level further depth can be achieved with relative ease but caution is in order (5) If planing is carried still deeper yellow nubbins which are lobules of subcutaneous fat are exposed This level is well below the sebaceous glands and at the depth of the deepest hair papillae Planing at this level is likely to result in removing so much adnexa as to cause scar formation

Results of experiments on the comparative effects of refrigerant on animal and human skin indicate that human facial skin can tolerate considerable freezing with ethyl chloride or dichlorotetrafluoroethane (Freon 114) but that mixtures containing large proportions of the much colder dichlorodifluoromethane (Freon 12) may be undesirable Refreezing an area of the skin to perform more adequate planing is not considered hazardous

One of the authors performed five full face planings on 3 patients with pitted acne scars who had typical keloids elsewhere on the body In each a small test area was first planed on the face then no untoward reaction having occurred in 6 weeks the full face was planed All 3 patients had an entirely satisfactory course over many months after planing

► [It is encouraging to learn that patients with acne scarring and keloids elsewhere on the body apparently may have their face planed without formation of keloids in that area Of course much additional experience in this regard is necessary —Eds]

treatment of superficial basal cell epithelioma by dermabrasion but others who have tried planing still prefer other methods of treatment The treatment of ordinary basal cell and squamous cell epitheliomas by planing needs further investigation It is certainly not the treatment of choice However it can be used safely in these lesions Perhaps planing plus irradiation will eventually give the best cosmetic result and the highest percentage of cures in superficial neoplasms It will never replace x irradiation, mutilating surgery or chemosurgery for far advanced growths Possibly the most important finding is that planing does not spread skin cancers Therefore it can be performed in the presence of epitheliomas

► [Apparently planing is the best available form of treatment for actinic and senile skin even though sometime senile keratoses may develop in the planed areas

To date there is no better method for the prophylactic care of precancerous skin Actually this could be a very important advance in dermatologic therapy and further experience with the method should be reported at intervals in the future

It is gratifying that no spreading occurred in the 32 cases of ordinary basal cell carcinoma treated by this method However one may ask whether the evidence from this survey material is sufficient to rule out the possibility of seeding malignant cells during the planing procedure from which epitheliomas will grow at a later date —Eds]

Recent Developments in Surgical Skin Planing are described by Samuel Ayres III J Walter Wilson and Ralph Luikart II (Univ of Southern California) Steel wire brushes have been largely replaced by the less hazardous diamond or ruby chip burs or fraises and serrated steel wheels The jet spray handpiece has been further improved Drawing its refrigerant liquid continuously from a tank containing more than needed even for prolonged operation it eliminates the time necessary for the operator to change from a hand held can to the abrading tool thus increasing the convenience and efficiency of the freezing planing procedure The jet spray handpiece has a spatter guard to protect the operator from the spray of abraded skin particles and blood similar devices are available to clip to the conventional handpiece

In addition to acne pits and wrinkling multiple actinic (senile) keratoses are an important indication for planing

(7) California Med 88 12 13 February 1958

Planing provides a nonscarring method for treatment of keratoses as well as a prophylaxis against skin cancer by replacing the sun damaged precancerous epidermis with new epidermal cells derived from the cutaneous adnexa Five depths of planing can be delineated during the planing procedure (1) first the pigment vanishes indicating that the major portion of the basal cell layer has been removed (2) myriads of yellowish macules less than 0 5 mm in diameter indicate that the upper dermis has been reached making the pilosebaceous apparatus visible (3) as planing goes deeper the surface appears studded with yellowish lobulated papules which are the sebaceous glands that have been cut across and is the depth usually achieved in moderately deep planing (4) if planing is carried deeper decided resistance of the tissues is encountered primarily because the tissue is below the penetration of freezing (about 2 mm) If freezing is done again at this level further depth can be achieved with relative ease but caution is in order (5) If planing is carried still deeper yellow nubbins which are lobules of subcutaneous fat are exposed This level is well below the sebaceous glands and at the depth of the deepest hair papillae Planing at this level is likely to result in removing so much adnexa as to cause scar formation

Results of experiments on the comparative effects of refrigerants on animal and human skin indicate that human facial skin can tolerate considerable freezing with ethyl chloride or dichlorotetrafluoroethane (Freon 114) but that mixtures containing large proportions of the much colder dichlorodifluoromethane (Freon 12) may be undesirable Refreezing an area of the skin to perform more adequate planing is not considered hazardous

One of the authors performed five full face planings on 3 patients with pitted acne scars who had typical keloids elsewhere on the body In each a small test area was first planed on the face then no untoward reaction having occurred in 6 weeks the full face was planed All 3 patients had an entirely satisfactory course over many months after planing

► [It is encouraging to learn that patients with acne scarring and keloids elsewhere on the body apparently may have their face planed without formation of keloids in that area Of course much additional experience in this regard is necessary —F I]

Dermabrasion Tattooing Preliminary Report is presented by Frank D Bernard[8] (Univ of Wisconsin) The technic is used in treatment of port wine stain hemangioma

METHOD—Under general anesthesia an Iverson dermabrader is used to remove the superficial layers of the epithelium Dermabrasion is carried only sufficiently deep to produce a denuded area to receive pigment Bleeding is controlled by warm saline packs and pressure While pressure is being applied the pigment is carefully mixed to obtain a good color match The pigment is suspended in saline to form a paste and when the denuded area is free of significant bleeding the preparation is applied evenly and rather heavily Fine mesh gauze followed by application of a pressure dressing completes the procedure The dressings are allowed to fall off as the denuded surface heals

Results in a small series have been sufficiently good to warrant further trial In some cases most of the lesion was covered by a permanent pigment layer with marked improvement Complete coverage of the hemangioma has not been achieved and probably never will be but the improvement gained allows the patient to disguise the lesion with a minimum of ordinary cosmetics Before the procedure can be advocated for general use the technic must be further developed so that the take of the pigment is more uniform Factors believed to influence the degree of take include depth of the lesion amount and character of the postoperative exudate on the wound surface depth of dermabrasion and amount of postoperative motion in the treated area

► [When referring to the therapy of port wine stain in the introductory paragraph the author states Application of radioactive material raises serious objections In our opinion this statement requires clarification While radium and superficial x rays are contraindicated in the therapy of this condition there is one form of radioactive material i e thorium X to which these objections do not apply Thorium X has been used in dermatologic practice for over 45 years so that by now there is considerable long term experience with this material One of its principal applications has been in the treatment of these port wine stains When applied according to accepted technics one can expect a favorable cosmetic response in about one third of the patients treated To our knowledge no sequelae of any consequence have resulted from the proper use of thorium X in the treatment of nevus flammeus —Eds]

Note on Treatment of Epitheliomas by Dermabrasion C M Ridley[9] (London Hosp) treated 11 patients 2 of them with radiodermatitis Initial results were successful The area planed included a margin of 2 5 mm normal skin In some cases 2% Xylocaine® with 1 80 000 epinephrine was

(8) Plast & Reconstruct Surg 2 6 0 September 1958
(9) Brit J Dermat 0 93 95 Aug Sept 1958

used as a local anesthetic instead of Arcton or Freon spray This made it easier to judge when small neoplastic areas had been adequately removed

One patient with radiodermatitis had been treated 3 years previously with rays for basal cell carcinoma in the lum bar region An ulcer with a raised edge in the center of the area of radiodermatitis proved to be basal cell carcinoma his tologically Further x ray treatment wa not feasible and exci ion would have meant extensive intervention and graft ing The other patient with radiodermatitis had had x ray and radium treatment for keratoses and epitheliomas of the face A triangular area involving the whole left side of the upper lip was particularly affected the skin showing atro phy pigmentation telangiectasia multiple small keratoses and a dome haped basal cell carcinoma After 3 dermabra ion treatments the skin healed completely

If there is no late recurrence the treatment will substitute 3 essions of mild inconvenience for hospitalization general anesthesia and extensive surgery The rate of healing was not significantly slower in areas of radiodermatitis than in other areas The healed areas were smooth and atrophic and le pigmented than before Healing was a little slower in 2 ca es of intraepidermal carcinoma on the external ear than in other lesion but ultimately the skin was sound and no carring was apparent

► [For obvious reasons it will not be possible to judge the efficacy of this un rthodox form of therapy until at least a 3 5 year period of observation ha elapsed —Eds]

New Treatment for Pitted Scars Preliminary Report is pre ented by Arthur S Spangler[1] (Harvard Med School)

Procedure —The area of scarring is anesthetized with 2% procaine solution using a 20-gauge needle A triangular 2-edged Bowman iris needle i in erted through the hole made by the procaine needle and the fibrous strand beneath the scar are cut by horizontal motions of the knife After bleeding has been partially controlled by pressure approximately 0 1 cc of a su pension of fibrin foam (17 mg /cc) i njected into the area beneath the scar The injection is made with 20-gauge needle inserted through the opening made by the procaine injection The opening i then partially clo ed by pre sure and cov ered with adhesive tape

A total of 23 patient with 255 deep pitted scar were treated An average of 0 1-0 2 cc u pension was used de

(1) A M A h De mat 08, 11 Decembe 19 7

pending on the size of the scar Results were uniformly good in obliterating depressions There has been no recurrence of *pitting in 74 scars treated with a single injection and ob*served 24 months Scars deep enough to cause loss of pilosebaceous orifices and atrophy of the epidermis remained visible because of contrast with surrounding normal skin but were much less conspicuous than previously

Most patients experienced no discomfort Rarely, slight aching or mild stinging was experienced but symptoms were promptly relieved by 10 gr acetylsalicylic acid There have been no serious side effects such as infection keloid formation or foreign body granuloma

► [The photographs in the original article show a very significant improvement in the appearance of the scarred area However until more experience has been gained one cannot rule out the possibility that a foreign body reaction might develop in the skin of some patients —Ed]

Chondrodermatitis Nodularis Chronica Helicis Nondeforming Surgical Cure for Painful Nodule of Ear is described by Murray C Zimmerman- (Univ of Southern California) The operation was devised on the assumption that the basic pathologic changes are primarily in the cutis They are secondary (if present at all) in the perichondrium cartilage or epidermis It is postulated that these changes are the result of chronic scarring from actinic or mechanical trauma This binds together the epidermis cutis and perichondrium into a firm unit Further trauma leads to edema in the bound down area with resultant pressure induced ischemia and possibly ischemic neuritis

The surgical approach has four aims (1) to cut the old adhesions which firmly bind down the epidermis and cutis on the perichondrium (2) to eliminate the mechanical squeezing of the dermis between perichondrium and epidermis leading to ischemic change (3) to remove existing reactive inflammatory tissue in the cutis perichondrium cartilage and epidermis at the chondrodermatitis site and (4) to cut the sensory nerves supplying the area for immediate relief of the characteristic pain

The surgical procedure is quick and easy and leave no postoperative deformity It can be done in one stage The author has treated 13 patients with no recurrences The only complications have been a small hematoma in 1 case and

( ) A M A Arch Derm 78 41 46 July 1958

temporary oozing at the incision site in another. No postsurgical chondritis or secondary infection has occurred.
► [The original article contains a detailed and illustrated description of the technic.—Eds.]

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2. ECZEMATOUS DERMATITIS (INCLUDING ALLERGIC), INDUSTRIAL DERMATITIS, ATOPIC DERMATITIS, URTICARIA

Lichenoid Eruptions Following Contact Dermatitis were observed by William R. Buckley[3] (Univ. of Rochester) in photographic operators handling certain p-phenylenediamines. These aromatic amines are used as color developers in the photographic trade and in making chemical intermediates, dye for furs and antioxidants for gasoline and rubber.

Contact dermatitis from exposure to aromatic amines in the photographic industry may be acute or subacute. In the acute type, an intense eczematous response occurs that shows histologically liquefaction of the basal layer in addition to the usual features of dermatitis. On subsidence of the acute eruption the residual lesions are lichenoid in type. In the subacute type, which accounts for over 90% of the cases observed, dry papular lesions develop slowly and are usually lichenoid from the beginning. If contact with the amines is sufficiently great or prolonged, the subacute process may evolve into the acute variety. A reddish purple or violaceous color is present throughout the acute or subacute skin reaction. Although the dry papules of subacute dermatitis and healing acute eruptions resemble lichen planus clinically and histologically, most microscopic sections show spotty parakeratosis and a more intense perivascular and adnexal infiltrate than is noted in true lichen planus. Pigmentary changes occur in the skin as healing of lichenoid eruptions continues. Such changes have not been permanent but may take a year or more for complete clearing in dark-complexioned persons.

Lichenoid eruptions after contact dermatitis occur only in sensitized persons. The hydrochloride salt of the substituted p-phenylenediamines when applied to the skin of a sensitized

(3) A.M.A. Arch. Derm. 78:454-457, Oct., 1958.

pending on the size of the scar Results were uniformly good in obliterating depressions There has been no recurrence of pitting in 74 scars treated with a single injection and observed 24 months Scars deep enough to cause loss of pilosebaceous orifices and atrophy of the epidermis remained visible because of contrast with surrounding normal skin but were much less conspicuous than previously

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The surgical approach has four aims (1) to cut the old adhesions which firmly bind down the epidermis and cutis on the perichondrium (2) to eliminate the mechanical squeezing of the dermis between perichondrium and epidermis, leading to ischemic change (3) to remove existing reactive inflammatory tissue in the cutis perichondrium cartilage and epidermis at the chondrodermatitis site and (4) to cut the sensory nerves supplying the area for immediate relief of the characteristic pain

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(2) A M A Arch Dermat 8 41-46 July 1958

the toxic principle of philodendron is water soluble and that it lies within the leaves rather than on their surface

A paradox in philodendron dermatitis is that it occurs frequently in workers in nurseries but seldom in housewives who handle the plants at home This probably can be explained by the fact that plants in the home are rarely touched whereas nursery workers may come in contact with cut leaves and stems hundreds of times a day Further in the home plants are watered at the base to avoid dripping and splashing but in a nursery they are watered so that the entire plant becomes wet

► [Other cases of philodendron dermatitis including several in housewives were reported by Ayres and Ayres (A M A Arch Dermat 78 330 1958) The reasons given by Dorsey explain why nonoccupational dermatitis due to this very common plant apparently is relatively rare —Eds]

Identical Skin Eruption in Five Men after Massive Exposure to Jellyfish (Aurelia) Aurelia or the saucer blubber usually does not cause injury to the skin when handled However Hanns Pacy (Tea Gardens New South Wales) reports the simultaneous appearance of an itchy papulovesicular eruption on the feet and ankles of 5 adult brothers 16 hours after contact with shallow water massively infested with a jellyfish seemingly of the genus Aurelia The papules were sharply defined arising out of unaffected skin pink in color and 4 8 mm in diameter In the center of the larger lesions were small vesicles containing serous fluid Internal and external antihistaminic treatment relieved the pruritus in the 3 more severely affected brothers but did not affect the 8 day course of the disease as compared with 2 controls treated with calamine lotion only

Stings of the larger jellyfish such as physalia (bluebottle) or brown blubbers are usually noticed immediately but these men noticed nothing until they awoke the morning after contact The larger jellyfish stings are painful but pain was entirely absent in these men The brothers all reported they had experienced similar eruptions 2 years previously after exposure to similar jellyfish which massively infested shallow water At that time the lesions lasted about 5 days

Contact Dermatitis Due to Thermofax Copy Paper Junji Hasegawa Fred Levit and Samuel M Bluefarb[6] (Chicago)

(5) M J Australia 2 580-58 Oct 19 1957
(6) J A M A 166 1173 Mar 8 1958

operator will produce an eruption that duplicates the lesions seen clinically The patch test is removed in 24 hours and the underlying skin is washed gently with an acid type skin cleaner to remove excess chemical which because of its proclivity to become fixed to epidermal cells might lead to sensitization by the patch test itself

Preventive measures to control contact dermatitis in the photographic industry include (1) proper selection of operators avoiding those with chronic skin disorders (2) proper training in handling of chemicals and good housekeeping in work areas (3) avoidance of actual contact with chemicals by use of mechanized chemical processing equipment rubber gloves and aprons, (4) removal of the chemicals *from the skin as soon as possible* and (5) *prompt* medical attention to operators who have had considerable skin contact with substituted p phenylenediamines

► [Neither allergic contact dermatitis due to p phenylenediamine and other aromatic amines nor lichen planus and lichenoid eruptions which *resemble lichen planus are rare What is unusual is the high incidence* of lichen planus like eruptions in a group of workers with allergic contact dermatitis due to this particular group of chemicals Buckley does not identify the exact p phenylenediamine compounds used in the plants that he investigated It is interesting that apparently one or several of these compounds have the capacity to produce lichen planus like eruptions —Eds]

Philodendron Dermatitis Clete Dorsey[4] (Univ of Southern California) reports a case

Mexican girl 23 worked in a commercial greenhouse A papulovesicular eruption involving the dorsa of both hands inner wrists and *forearms and outer surfaces of the upper arms started 2 weeks* after she began planting philodendron cuttings Her eyelids face and neck were diffusely swollen and erythematous A patch test was negative after 24 hours but when the crushed leaves and stems used for testing were moistened with water the test became positive at 48 hours Patch tests with other plants handled by the patient were negative

Three other persons worked at the nursery where the patient was employed The owner and his wife were allergic to philodendron but a Mexican gardener was not Of 6 other commercial nursery owners who were interviewed 2 reported a high incidence of philodendron sensitivity among their workers They reported that the plants were more troublesome when the leaves were wet This observation plus the fact that the present patient showed a positive patch test reaction only after the leaves were moistened suggest that

(4) California Med 89 329 330 April 1958

touch the paper when the hand rests while making notes

Since there is no known method of desensitization cure can be attained by a change of job or a change of paper Non allergenic papers are now available for one type of machine—Minnesota Mining and Manufacturing Company Thermofax Duplicator papers DPX 12 88 J1 (buff tinted) and DPX-26-36-J10 (white) Exposure to even a pencil contaminated by touching one of the allergenic papers is enough to cause the eruption to relapse so a complete office changeover to the new paper seems the only solution

► [Dermatitis due to Thermofax duplicating paper has been reported from many parts of the United States (Standish M Connecticut M J 22 363 1958 Cipollaro A C AMA Arch Dermat 77 334 1958 Kendrick F J ibid p 334 Domonkos A N ibid p 625 Silverberg M C ibid p 741 and Fisher A A ibid p 741) It is our understanding that the chemical previously responsible for the allergic contact dermatitis from Thermofax paper has been changed but sensitivity to this new paper apparently has already been observed.—Eds]

Eczematous Sensitization to Neomycin and Bacitracin was observed by V Pirila and T Wallenius[8] (Univ of Helsinki) during a 20 month period in 28 patients on whom the two drugs were used simultaneously in the same ointment This combination was used in treating infectious eczema in 27 patients and burns in 1

In 25 patients an epicutaneous test was performed with the various components of the ointment used All 25 responded to neomycin and 18 to bacitracin but none to the ointment base materials The reactions often developed only 3 5 days after the test which might be due to the poor absorption of the antibiotics through the skin

Many patients were allergic to neomycin and to bacitracin Such widespread hypersensitivity to two different substances could hardly be considered as a simultaneous true heterogeneous sensitization against neomycin and bacitracin particularly as no isolated hypersensitivity to bacitracin alone was observed among the study patients The hypersensitivity to neomycin was about 10 times stronger than to bacitracin These observations suggest that the neomycin and bacitracin compounds available to the authors *might* have contained a mutual or closely related substance(s) which caused the sensitization The existence of such a com

(8) *Hautarzt* 8 3 8-519 November 1957

report 2 cases of this one of which is described here

Man 63 had severe dermatitis of the face palms dorsum of the hands and wrists which appeared 1 week after he received 2 injections of penicillin for an ear infection A patch test with 5% solution of nickel nitrate was positive Ten days after leaving the hospital he had a recurrence of the dermatitis He then recalled using a Thermofax duplicating paper at work for several weeks before the first attack of dermatitis Patch tests with this copy paper in both its preprocessing and postprocessing state were strongly positive A patch test with a special hypoallergic Thermofax paper was also positive Patch tests with four types of plastic material potassium dichromate hatband material basic chromium sulfate bichloride of mercury, copper sulfate cobalt nitrate and Remington Rand Transcopy paper were negative

The Thermofax process uses a particular type of paper which is simultaneously subjected to heat, light and pressure while in close contact with the page being duplicated After a few seconds exposure a direct positive image is obtained and the copy may be used immediately The allergenic material in the Thermofax paper is reported to be a tertiary butyl catechol compound The authors patch tested patients with other forms of dermatitis using Thermofax copy paper and obtained negative results

Contact Dermatitis from High Speed Duplicator Papers New Disease of Office Workers Charles Sheard Jr Herbert J Spoor and Robert Abel[7] (Cornell Univ) report 5 cases The cause is a type of sensitized paper used in a new high speed duplicating machine in which the paper is inserted in the machine along with the sheet to be copied and is exposed to intense light The chemical in the paper is a trade secret but the authors were informed that it is a simple chemical

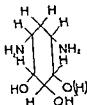
The eruption is severe with vesiculation erythema and seborrhea like superficial scaling It characteristically seems to involve the lower lip a site invariably affected in smokers Messengers exhibit the eruption on the knuckles where they touch the paper when they carry bundles of it with fingers under the string or on the ulnar forearms or leaned-on areas Businessmen often have the eruption on the first 3 fingers of both hands where they touch the paper when turning pages and folders or on the ulnar right palm where they

(7) A M A Arch Dermat 77 435 43 April 1958

instances ordinary patch testing was insufficient to elicit a reaction However light scarification of the area before testing regularly yielded positive results in sensitized patients

Neomycin obtained from Streptomyces fradiae is a mixture of neamine and two glucosides of this substance

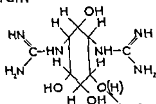
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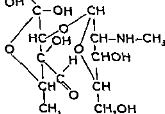
NEAMINE BIOSAMINE

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STREPTOMYCIN



STREPTIDINE



STREPTOBIOSAMINE

Fg n (S 1 F I J I est D rm t 30 2 5 231 M y 19 8)

Framycetin a closely related antibiotic is another neamine glucoside The common neamine moiety is a cyclohexane bearing two amino groups (Fig 2) The glucide fractions 1 neomycin B and C and framycetin are probable bioses bearing an amino group The formula of streptomycin (Fig 3) also consists of a substituted cyclohexane (streptidine) linked to an amino substituted biose (streptobiosamine)

mon component is quite possible The neomycin compound consists of three components neomycin A B and C the relative amount of each component varying with the different neomycin preparations Furthermore the preparations also contain some contaminants The composition of bacitracin is not yet clarified According to Jawetz bacitracin preparations sold in the United States contain about 20% contaminants

► [Since allergic eczematous contact sensitization to bacitracin alone is very uncommon the most reasonable assumption would be that neomycin was the primary allergen in these cases with secondary (cross) sensitization to bacitracin This would presuppose that immunochemically identical or similar groupings are present in neomycin and bacitracin unless the contaminants mentioned by Firth and Wallenius play a role Further support comes from a publication by Niels Hjorth on overtreatment dermatitis due to neomycin bacitracin ointments (Ugesk laeger 120 1373 1958) He also reported a high incidence of sensitization to both neomycin and bacitracin

It is puzzling that to our knowledge even though a number of preparations combining neomycin and bacitracin have been sold in the United States for several years there has been no obvious increase in sensitization to this combination of antibiotics —Eds]

Cross Sensitization between Neomycin and Streptomycin During the first year of use of neomycin Edwin Sidi Marc Hincky and Robert Longueville[9] (Paris) observed no sensitizations Only after reapplication of neomycin in patients treated with it several months previously did a number of cases of sensitization appear During investigation of a case of eczema due to contact with neomycin it was found that the patient had become extremely sensitive to streptomycin As this patient had had no previous contact with streptomycin it was decided to test all further patients sensitized to neomycin or streptomycin with both compounds It was found that patients sensitized to either one are regularly sensitive to the other

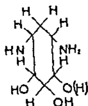
To date 8 such cases have been observed Five of the patients with positive patch tests to both antibiotics had never had contact with streptomycin Two had no known contact with neomycin but had been handling streptomycin One patient had contact with both antibiotics and reacted with an anaphylactoid response to an intramuscular injection of streptomycin followed by eczematization of neomycin treated areas In every case reaction to streptomycin was markedly more positive than to neomycin In a number of

(9) J Invest Derm 30 ? 231 May 1958

instances ordinary patch testing was insufficient to elicit a reaction However light scarification of the area before testing regularly yielded positive results in sensitized patients

Neomycin obtained from Streptomyces fradiae is a mixture of neamine and two glucosides of this substance

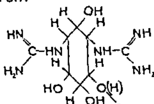
NEOMYCIN



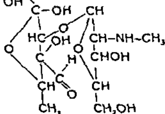
NEAMINE BIOSAMINE

Fig (Court of Sd E / J I t D rm t 30 5 31 M 19 8)

STREPTOMYCIN



STREPTIDINE



STREPTOBIOSAMINE

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The chemical configuration causing cross sensitization between neomycin and streptomycin is likely to be found in the aglycone moieties, but the exact chemical group responsible for this phenomenon has not been ascertained

The type of reaction seen after topical sensitization to antibiotics seems somewhat different than that in the usual allergic contact dermatitis Instead of an acute vesicular oozing process, the reaction is often of the dry desquamative spreading type which may at times involve covered areas more suggestive of atopic dermatitis The necessity for scratching the skin area to be patch tested to obtain reproducible results seems to indicate a deeper site of reaction than in the usual contact dermatitis

► [The following facts concerning allergic sensitization to neomycin have come to be recognized recently (1) Sensitization to this antibiotic is not particularly uncommon (2) Cross sensitization to streptomycin and perhaps also to bacitracin is not uncommon (3) Allergic sensitization sometimes cannot be demonstrated with the conventional patch test in such instances intracutaneous tests for the delayed 48 hour reaction (Epstein S Dermatologica 115 596 1957) or patch on scratch tests are necessary to show the existence of allergic sensitization (4) Clinically allergic sensitization to neomycin can become manifest either as a subacute erythematosquamous or an acute papulovesicular eruption —Eds]

Persistence of Allergic Eczematous Sensitivity and Cross Sensitivity Pattern to Paraphenylenediamine Paraphenylenediamine (PPD) is a frequent and potent sensitizer producing many cases of allergic eczematous contact dermatitis It is used principally in hair and fur dying It may cross react with other chemicals having an amino grouping in the para position in the benzene ring including certain dyes local anesthetics para aminobenzoic acid (PABA) and the sulfonamides

Alexander A Fisher Alfred Pelzig and Norman B Kanof[1] (New York Univ Post Grad Med School and Skin and Cancer Unit) found that 46 of 50 patients with strong hypersensitivity to PPD retained this sensitivity for 3 10 years Of the 46 PPD reactors 11 gave cross reactions to benzocaine 4 to procaine and benzocaine 3 to PABA and benzocaine and 1 to sulfanilamide

Several PPD positive women in this study repeatedly exposed themselves to PPD in hair dyes without any increase in PPD sensitivity as measured by patch tests The exposures always caused a severe dermatitis but these patients

(1) J Invest Dermat 30 9 1 January 1958

showed no widening of their spectrum of sensitivity Repeated patch testing of these PPD positive patients with other compounds containing the para aminobenzyl group did not sensitize them to the other compounds

The study indicates that PPD sensitivity once established persists for years The spectrum of cross sensitivity to PPD appears to be related to an individual host factor and to be established early

► [The persistence of PPD sensitivity in 46 of 50 patients is in conformity with current knowledge Allergic eczematous sensitivity to certain other allergens (e g nickel) according to reports published in recent years is apparently more readily lost. The new finding in these studies is that there was no widening of the cross sensitization pattern despite repeated exposures to the primary allergen which were sufficiently intense to produce severe dermatitis as well as exposures to potential secondary allergens We believe that more extensive studies on this important problem are indicated.—Eds]

Contact Dermatitis from Vitamin B_1 (Thiamine) Relapse after Ingestion of Thiamine Cross Sensitization to Co Carboxylase Niels Hjorth (Finsen Inst Copenhagen) reports a case of occupational dermatitis due to thiamine in a girl 17 Relapses of the dermatitis occurred after ingestion of 200 mg thiamine and later after intracutaneous injection of 10 mg Patch tests with pure crystalline thiamine were positive even in 0 1% dilution

The thiamine molecule is comprised of a thiazole and a pyrimidine component After intestinal resorption the thiamine is esterified with pyrophosphoric acid and thus changed to co carboxylase which is a coenzyme in cellular metabolism Part of the ingested thiamine is eliminated in the urine as a pyrimidine derivative

The decomposition products have not been tested in any of the previously reported cases of hypersensitivity to thiamine Sensitization to these products might occur since thiamine is unstable at the prevailing pH of the skin surface Patch tests with the thiazole component of thiamine were negative Patch tests with the pyrimidine component pure and 1 in 10 [illegible] dilution were positive on one occasion but tests with 10 [illegible] and 1 [illegible] dilutions were negative 2 days later As thiamine elicited reactions even in 0 1% solution it is unlikely that the decomposition products could be the primary allergen

[illegible] 37 612 4 May 19[illegible]

The chemical configuration causing cross sensitization between *neomycin and streptomycin is likely to be found in* the aglycone moieties but the exact chemical group responsible *for this phenomenon has not been ascertained*

The type of reaction seen after topical sensitization to antibiotics *seems somewhat different than that in the usual* allergic contact dermatitis Instead of an acute vesicular *oozing process, the reaction is often of the dry desquamative* spreading type which may at times involve covered areas *more suggestive of atopic dermatitis The necessity* for scratching the skin area to be patch tested to obtain reproducible *results seems to indicate a deeper site* of reaction than in the usual contact dermatitis

► [The following facts concerning allergic sensitization to neomycin have come to be recognized recently (1) Sensitization to this antibiotic is not particularly uncommon (2) Cross sensitization to streptomycin and perhaps *also to bacitracin is not uncommon* (3) Allergic sensitization sometimes cannot be demonstrated with the conventional patch test in such instances intracutaneous tests for the delayed 48 hour reaction (Epstein S *Dermatologica 115 596 1957*) or patch on scratch tests are necessary to show the existence of allergic sensitization (4) Clinically allergic sensitization to neomycin can become manifest either as a subacute erythematosquamous or an acute papulovesicular eruption —*Eds*]

Persistence of Allergic Eczematous Sensitivity and Cross *Sensitivity Pattern to Paraphenylenediamine* Paraphenylenediamine (PPD) is a frequent and potent sensitizer producing *many cases of allergic eczematous contact* dermatitis It is used principally in hair and fur dying It may cross react with other chemicals having an amino grouping in the para position in the benzene ring including certain dye local anesthetics para aminobenzoic acid (PABA) and the sulfonamides

Alexander A Fisher Alfred Pelzig and Norman B Kanof[1] (New York Univ Post Grad Med School and Skin and Cancer Unit) found that 46 of 50 patients with strong hypersensitivity to PPD retained this sensitivity for 3 10 years Of the 46 PPD reactors 11 gave cross reactions to benzocaine 4 to procaine and benzocaine 3 to PABA and benzocaine and 1 to sulfanilamide

Several PPD positive women in this study repeatedly exposed themselves to PPD in hair dyes without any increase in PPD sensitivity as measured by patch tests The exposures always caused a severe dermatitis but these patients

(1) J Invest Dermat 30 9 12 January 1958

showed no widening of their spectrum of sensitivity Repeated patch testing of these PPD positive patients with other compound containing the para aminobenzyl group did not sensitize them to the other compounds

The study indicates that PPD sensitivity once established persists for years The spectrum of cross sensitivity to PPD appears to be related to an individual host factor and to be established early

► [The persistence of PPD sensitivity in 46 of 0 patients is in conformity with current knowledge Allergic eczematous sensitivity to certain other allergens (e g nickel) according to reports published in recent years is apparently more readily lost The new finding in these studies is that there was no widening of the cross sensitization pattern despite repeated exposures to the primary allergen which were sufficiently intense to produce severe dermatitis as well as exposures to potential secondary allergens We believe that more extensive studies on this important problem are indicated.—Eds]

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1 1 Dermat 33 61 264 M y 19 8

Though the pyrimidine derivative used for the tests (2 methyl-6 amino 5 brom methyl pyrimidine) is a primary irritant the reactions provoked by it might be an expression of a cross sensitization or secondary allergy provided the pyrimidine part was the antigenic determinant group of the thiamine molecule This cross sensitization in that case should occur with amino methyl pyrimidine However tests with this compound were negative Thus the observed reactions with the pyrimidine component of thiamine must have been due to the primary irritant properties of the substance and it may be concluded that the primary allergen in this case was the whole thiamine molecule A secondary allergy to co carboxylase was indicated by positive patch tests to 10% and 1% dilutions This seems to be the first demonstration of a hypersensitivity to a pure coenzyme

► [The first demonstration of allergic hypersensitivity to a coenzyme but only one of many now known allergic sensitivities to body own substances The question arises why this patient remains clinically well when she is exposed to exogenous thiamine from food as well as exposed uninterruptedly to thiamine from her endogenous co carboxylase The answer in all probability lies in the fact that even in allergic hypersensitivity the size of the exposure is an important factor There is simply not enough thiamine available from food and coenzyme to elicit a clinically recognizable reaction in the skin —Eds]

Local Allergic Edema Induced by Injected Procaine Diagnostic Value of 24 Hour Intracutaneous Test Sheppard Siegal[3] (Mount Sinai Hosp New York) observed 3 patients who had repeated reactions to procaine characterized by marked swelling of the cheek and face at the site of injection of the drug for dental anesthesia There was no evidence of general reaction or urticaria In each instance a preliminary impression of infection or trauma as a cause of the edema had to be discarded Allergy to procaine was demonstrated by a skin test reaction of the delayed 24 hour type to intracutaneous injection of the drug In each case skin tests with monocaine were also positive Skin tests with Xylocaine were negative The latter anesthetic is sufficiently distinctive in chemical structure so that cross sensitization is unlikely It is a safe substitute for procaine

The phenomenon of local allergic edema due to injected procaine is not widely recognized Although procaine has been in use for over half a century reports of this type of al

(3) J Allergy 29 329 335 J ly 1958

lergic reaction have appeared only in recent years Such reactions may be more frequent because of the widespread use of procaine penicillin since 1948 This slowly absorbed depot preparation contains procaine in 12% suspension and may be a more potent sensitizer than the usual procaine solution This possibility is suggested by a concomitant positive penicillin 24 hour type skin test in 2 of the 3 patients with procaine edema Two other patients with penicillin allergy were shown to have a positive 24 hour skin te t with procaine

► [Th s study provides a reasonable explanation for local reactions to procaine which are not too unusual and which hitherto have been unsatisfactorily interpreted as due to infection Further it presents a practical technic for establishing whether delayed procaine sensitivity exist in a patient The lack of cross sensitization between Xylocaine and procaine on intradermal testing parallels the findings in allergic ec cu tions sensitivity t procaine —Eds]

Allergic Origin of Zirconium Deodorant Granulomas was demonstrated by Walter B Shelley and Harry J Hurley[4] (Univ of Pennsylvania) A standard commercial zirconium stick deodorant was rubbed in the left axilla for 5 minutes every morning by 30 men After 1 month a chronic noninflammatory eruption appeared in the axilla of 1 man Two weeks later biopsy showed an early epithelioid granuloma At 10 weeks biopsy showed a fully formed granuloma of many epithelioid cells some giant cells and a few inflammatory round cells The right axilla of all subjects was treated at the same time with a stick identical with the deodorant stick except for the ab ence of zirconium No gross or microscopic change were ob erved in any subject as a result of this application Thus repeated topical application of stearate hexachlorophene carbitol alcohol and perfume produced no granulomas

After completion of the foregoing experiment the subjects applied 0 5 odium zirconium lactate in sodium stearate alcoh l and water to the right axilla for 5 minutes daily for 10 week S dium zirconium lactate 10% in sodium stearate alc h l and water was applied to the left axilla One subject exhibited typical granulomatou changes in the axilla treated with the 10% concentration after application for 1 m nth Thus sodium zirconium lactate in a plain sodium tearate soap vehicle can produce the typical granulomatous

(4) R t J Dermat 0 5 101 M h 1958

response which was observed clinically after use of deodorant sticks containing zirconium

Patch tests with zirconium deodorant were uniformly negative in the 2 men with axillary granulomas and in 20 normal controls However, with intradermal testing the men with axillary granulomas showed a unique granulomatous response to the introduction of dilute aqueous solutions of sodium zirconium lactate All areas of skin were reactive The controls showed *no response Injections of* zirconium chloride and zirconium nitrate were as granulomagenic as injections of sodium zirconium lactate in the subjects with positive tests, whereas injections of beryllium sulfate and colloidal silica produced no response It is thus apparent that the 2 men who acquired deodorant granulomas in the experimental studies had a specific hypersensitivity reaction to the zirconium which manifested itself as a granuloma In 1 of these intradermal injection of 0 02 ml of 1 10 000 zirconium solution produced a granuloma in the other 0 02 ml of a 1 1000 dilution caused a reaction

In another subject not part of the experimental study the authors observed acquisition of zirconium hypersensitivity Initial tests for zirconium were *repeatedly negative* Month later the test sites showed a granulomatous reaction Further tests with zirconium proved that the subject had become specifically sensitive to zirconium

Patch tests with zirconium stick deodorant were negative in 4 patients who had clinically typical deodorant granuloma of the axillae from use of zirconium deodorants All 4 were sensitive to intradermal injection of 0 02 ml of 1 1000 sodium zirconium lactate and 3 were sensitive to a 1 10 000 dilution

Though certain *granulomas have been suspected of being* allergic in origin this is the first direct demonstration in man that the introduction of extremely small amounts of a pure substance may produce a delayed allergic reaction in the form of an epithelioid granuloma This is an entirely new facet of immunologic response that must be explored in relation to all granulomatous processes Intradermal skin testing must extend to discover and identify granulomagenic allergens which may be operative in such diseases as leprosy sarcoidosis and tuberculosis Intradermal skin testing of pa

tients with beryllium silicate and tattoo granulomas should afford rapid demonstration of specific hypersensitivity to the causative element

The quantitative aspects of the allergic granuloma are of a new order of magnitude Unbelievably small amounts of zirconium may elicit a granuloma As little as 0.2 µg sodium zirconium lactate was able to produce a small but grossly visible skin lesion in 1 patient In the search for the cause of granulomatous disease agents such as fatty acid which are needed in milligram quantities to produce granulomas need no longer be looked for Instead agents which act in microgram quantities must be sought The sensitized patient can respond to traces of an allergen well beyond the point which can be detected by present day physical and chemical analytical procedures This accounts for the failure of previous workers to demonstrate zirconium in axillary granuloma specimens

These studies indicate that the granulomatous response is due to the zirconium ion and not to any particular salt or to an impurity No cross sensitization phenomena have been encountered as yet but the possibility of cross sensitivity to other elements such as its twin hafnium must be borne in mind

► [These studies confirm what had been suspected clinically *namely* that the zirconium in stick deodorants was the cause of the axillary granulomas seen *in the United States in 1956-57* However probably not all cases can be explained on this basis since some patients *with* axillary granulomas denied having used one of these sticks

That these granulomas are of allergic *origin is most* interesting and also explains why only relatively few among the *multitudes* who used zirconium containing deodorant sticks developed granulomas The finding of a granulomatous *response histologically* does not come as a surprise The early histologic *response* at the intradermal test site in the tuberculin type of allergy is composed mainly of *mononuclear cell* but after weeks and months epithelioid cell formation is *observed* It appears possible e g that if Epstein (A M A Arch Dermat 73 326 1956) had examined histologically the site of *delayed dermal* reaction to nickel and chromate after several months he would have *encountered* similar granulomatous changes Granulomatous alterations of allergic origin occurring after a positive patch test with beryllium sulfate in beryllium disease were previously reported by Sneddon (Brit M J 1 1448 1955) —Eds]

Asbestos Granulomas and Warts P Vulcan and St Tanasescu[5] report a case

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(5) Dermato-venerologia 3 21 Jan-Feb 1958

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(5) Dermato-venerologia 3 21 J F b 1958

dust Six months previously she had injured her right hand The wound healed within 2 months but a small firm hyperkeratotic nodule formed at the site of injury At about the same time several small wartlike lesions appeared on the dorsal surface of the fingers

Biopsy of the nodule on the internal margin of the right hand revealed acanthosis and hyperkeratosis of the epidermis with areas of pseudoepitheliomatous hyperplasia There was an infiltrate in the der

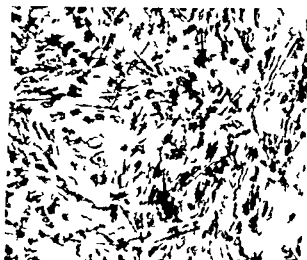


Fig 4 —H t o-fit l la t epith l d filt t on w th many le to cry t l (Courte y f V lcan P a l Tan esc St D t e rolog 3 21 Ja Fet 1958)

mis consisting of histiocytes epithelioid cell and fibroblast Among the cellular element were needle like birefringent crystal of varying size occurring singly and in groups (Fig 4)

The granulomatous infiltrate in this case resulted from the presence of minute particles of asbesto in the skin Asbesto is a hydrated magnesium silicate occurring in the form of soft slightly elastic threads Cutaneous granulomas may result from penetration of the skin by amorphous or crystallized silicon hydrated magnesium silicate aluminum silicate (kaolin) or complex polysilicates (mica feldspar amianthus asbestos) A variable period of latency usually occurs between the time of trauma and appearance of a cutaneous nodule

Examination of 25 women factory workers handling asbestos revealed wartlike lesions in 12 Clinically the lesion resembled simple warts with a predilection for the palmar aspect of the fingers especially at the interphalangeal folds

On biopsy some showed acanthosis and hyperkeratosis without evidence of cellular infiltration in the dermis or presence of asbestos needles The authors believe such lesion result from intraepidermal penetration of asbestos particles which are subsequently eliminated without penetration of the dermis

► [The studies of Shelley and Hurley indicate that cutaneous granulomas f this variety may be of allergic origin (see previous abstract) —Eds]

Chrome Dermatitis Study of Chemistry of Shoe Leather with Particular Reference to Basic Chromic Sulfate is presented by George E Morris[6] (Boston) The physician in attempting to elicit the cause of an eruption of the feet has been guided for years by certain accepted dicta (1) that the chromium used in tanning most shoe leather cannot cause such eruptions because it is not hexavalent and only hexavalent chromium can cause skin disease and (2) that the chromium is firmly fixed in the leather and cannot be removed easily Recent research has demonstrated that each of these long taught principles is incorrect

Leather chemists have established that chrome salts can be leached from shoe leather by the lactic acid and lactate in human perspiration These salts can thus be deposited on the skin The particular salt deposited by the tanning industry in hide fibers and fibrils is a basic chromic sulfate A representative compound of this type the one third basic chrome sulfate $[Cr(H_2O)_5OH]SO_4$ was recently made available to the medical profession for patch testing as was a chromic lactate complex containing 2 lactate ions per atom of trivalent chromium

Four cases of shoe leather dermatitis are reported in which the patients had positive patch tests to 0.2% basic chromic sulfate Two leather workers who previously had chrome dermatitis also had positive tests to this compound Another patient had a positive test to sodium dichromate but a negative test to basic chromic sulfate Chemical analysis of a nurse's stocking (whose shoes had shown green chromium discoloration) revealed large quantities of trivalent chromium

Positive patch tests to a trivalent chromium compound have not been reported previously Patients have been tested

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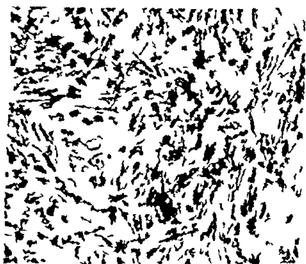


Fig 4 H[illegible]o-fibroblast[illegible] [illegible] infiltration with [illegible] (Courtesy of Vulcan [illegible] Tan[illegible] St[illegible] Dermat[illegible] Jan Feb 1958)

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tion of the skin by jewelry the author patch tested 8 volunteers with metal samples representing the composition of ring jewelry No reactions occurred with pure gold silver (900 fineness—87 5% silver 2 5% copper pure copper pure nickel 10 carat gold (9 parts gold 5 parts copper) nickel silver (75% nickel 25% copper) or silver copper (60% silver 40% copper) However metal corrosion was noted in all cases with pure copper and silver copper and in 1 instance with silver 900 fineness

Tests were then repeated with the addition of a sprinkling of table salt (3 5 mg) placed in the central opening of the washer shaped metal samples Erythematous and vesicular reactions occurred in 5 patients with silver containing 2 5% copper in 7 patients with pure copper in 7 patients with silver copper and in 1 patient with 10 carat gold One subject showed a delayed follicular erythema when tested with pure gold The reason for this reaction is obscure as is the paucity of reactions to 10 carat gold In 8 subjects marked metal corrosion was observed with silver containing copper and with pure copper Such corrosion also occurred in 7 instances with silver copper

It is concluded that in the presence of an adequate concentration of salt a primary irritant is produced when copper or copper alloy in silver is in contact with the skin Irritation from rings seems commoner than from other metal contacts on the skin The hands have many opportunities for exposure to loose salt and psychic and thermal sweating can deliver to the skin surface sufficient sodium and chloride ions to attack metal when concentration results from evaporation A thorough study of jewelry metal might produce alloys sufficiently inert to be nonreactive in the presence of varying salt concentrations on the skin surface

[In eczematous eruptions involving the ring area many factors may contribute to the development of the eruption besides the metals in the ring itself Soaps and other detergents waxes polishes oil chemical cleansers and other substances used in the house or occupation may accumulate under the ring and produce a local eruption unless the ring is cleansed at regular intervals Gaul's investigations demonstrate that salt can be another contributory factor making the metal a primary irritant However the negative patch tests do not entirely exclude the possibility of allergenic action of these metals in Gaul's cases As was shown by Epstein, in some cases of allergic dermatitis due to nickel and other compounds a positive delayed intracutaneous test reaction can be elicited whereas the patch test may be negative —Eds]

with ammonium or potassium dichromate (which are hexavalent) chromium acetate chromium chloride chromium phosphate, chromium carbonate chromium nitrate chromium oxide or chromium fluoride The author when looking for the cause of shoe leather dermatitis found no report in the literature of positive tests to these chemicals Negative results would be expected since these chromium compounds are not found in shoe leather This is the first report on patients suspected of having shoe dermatitis who were tested with the actual chrome salt found in their shoes

Case of Contact Allergy to Copper and Zinc is reported by B J Van der Meer[7]

Man 41 a technical worker for the telephone service had recurrent attacks of eczema principally on the legs which responded to ACTH *injections and bed rest He complained of itching in the elbow crease* which was covered with a zinc ointment dressing The next morning this area only was inflamed In his work he had contact with zinc but more with copper wire The ointment contained both zinc oxide and *zinc sulfate and also traces of copper 0 2 or 0 1/1 000*

Three metal plates 5×5 cm and 1 2 mm thick of copper brass and zinc were applied to the forearm After 24 hours a contact dermatitis had developed reaction to copper and brass was severe and to zinc less so but still definite Patch tests were then made with solutions of zinc sulfate in dilution of 10 1 0 1% and of copper sulfate 1 0 1 0 01 0 001 and 0 0001% Zinc produced a reaction with 1% and copper with 0 01% Analysis of the zinc sulfate showed traces of copper of not less than 0 00001% Nickel sulfate 0 5% and potassium bichromate 0 5% produced no skin reaction

Although the reaction to copper was 100 times as great as to zinc it was *concluded that the patient had a true contact* allergy to both metals

► [It would be interesting to know the result of patch tests on this patient with the zinc ointment that was used in the dressing as well as with zinc oxide itself It is difficult to rule out the role of copper contamination of the various preparations used here for patch testing —Eds]

Ring Dermatitis Primary Irritation from Action of Salt on Jewelry Alloys According to L Edward Gaul[8] (Evansville, Ind), patients are frequently seen with dermatitis under and around rings or dermatitis of the ear lobes back neck chest, shoulders wrist or lower abdomen where metal contact presupposes a metal sensitivity In many instances patch tests with metals are negative

In a search for possible accessory factors related to irrita

(7) Nederl tijdschr geneesk 101 166?-167 N 16 195
(8) A M A Arch Dermat 77 5 6-531 May 19 8

Epoxy Resins Their Uses and Chemical and Dermatologic Aspects are described by George E Morris[1] (Boston) Introduced in 1946 epoxy resins are now widely used in industry With their use have come severe dermatologic problems for the chemicals in these resins are sensitizers and irritants Epoxy resins chemically known as ethoxylene resins are polyethers with terminal epoxide groups Epoxies are available in a wide range of viscosities from low viscosity liquids to high melting point solids Many curing agents and additives used in preparing epoxy resins are severe skin irritants and sensitizers

The initial development of epoxies in the United States came from research in the paint industry The qualities of resistance to chemicals and to corrosive substances and fumes of durability and of flexibility have resulted in various and expanding uses of epoxy based surface coatings Epoxies also contain such strong adhesive qualities that they can effectually bind together many different materials including steel aluminum brass glass plastics ceramics rubber and wood Since some epoxies are fluid at room temperature they are used to make parts having thin sections and to fill molds containing fragile inserts The high insulation resistance of epoxy resins under extreme relative humidity and temperature changes has made them admirably suited for potting and encapsulating (i e sealing of sensitive electric parts in plastic blocks) Besides their importance in the electric automotive and aircraft fields the over all use of epoxies in television and electronics is constantly expanding They are also used in the manufacture of nonmetal tools and dies in the field of reinforced plastics and in many other industries

Dermatitis resulting from contact with epoxy resins is most commonly seen in the central third of the face the nose adjacent area of the cheeks upper lip and eyelids The forearms and hands are also commonly involved and sometimes the conjunctiva is irritated

Workers in industries using epoxy resins often are unaware that they are handling chemicals which can irritate the skin Although the main manufacturers of epoxies have warned of their dermatologic hazards many workers who

(1) A.M.A. Arch. Derma 6 75 61 December 19

Studies in Contact Dermatitis II Lipstick Cheilitis According to C D Calnan and I Sarkany [9] lipstick cheilitis accounts for more than half the cases of dermatitis due to cosmetics Of 110 cases observed during 4½ years 96 involved the vermilion border of the lips only The angle of the mouth are usually spared because most women do not apply lipstick to the corners of the lips

Fluorescein dyes are the only important cause of allergic sensitivity to lipsticks Indelibility cannot be achieved without the use of halogenated derivatives of fluorescein (eosin) The eosin actually combines with the keratin of the stratum corneum Almost all patients with lipstick cheilitis can use a fluorescein free lipstick Such lipsticks are not indelible but are otherwise satisfactory

Occasionally patients with lipstick cheilitis show a negative response to patch tests with eosin in low concentration This has been used as evidence of localized allergic sensitivity or photosensitivity The authors believe however that such test results are false negatives due to the fact that too *little allergen has penetrated the stratum corneum* The horny layer on the skin of the back or limbs is moderately thick whereas that on the vermilion border of the lips is extremely thin Eosin combines with keratin in an acid pH Hence small amounts of the dye can be immobilized by the keratin of the stratum corneum Only in high concentrations will there be enough dye to saturate the keratin and penetrate deeper to react with the antibodies and produce a reaction

Because of false negative patch test reactions with low concentrations patch tests with 50% eosin are recommended Most patients with lipstick cheilitis will have positive reactions to their own eosin containing lipstick and to 50% eosin and negative reactions to noneosin lipstick Such patients are advised to use noneosin lipsticks thus avoiding further trouble

► [Obviously lipstick cheilitis is much more common in London than in New York Cases of lipstick dermatitis represent only a very small percentage of our patients with allergic cosmetic dermatitis The reasons for this discrepancy in incidence are not immediately evident The finding that indelible *fluorescein dye* usually are the cause of these eruptions confirms the original work of Sulzberger and J Goodman (Arch Dermat & Syph 37 597 1938) —Ed]

(9) Tr St John H [illegible] D [illegible] 1957

Studies of Mechanism of Allergic Eczematous Contact Dermatitis II Use of C^{14} Labeled 2 4 Dinitrochlorobenzene in Guinea Pigs Victor H Witten and Cyril H March[3] (New York Univ Post Grad Med School and Skin and Cancer Unit) used radioactively tagged dinitrochlorobenzene 1 C^{14} (DNC^{14}B) to challenge (1) guinea pigs previously sensitized with nonradioactive dinitrochlorobenzene (DNCP) and (2) nonsensitized control animals Distribution and localization of the allergen or its metabolites in various tissues as evinced by the presence of radioactivity was ascertained by use of the Van Slyke Steele Plazin method of carbon combustion and proportional counting

Definite differences in the amount of radioactivity found in sensitized and control guinea pigs after challenge with DNC^{14}B were noted in 2 of the 7 tissues studied the skin and the buffy coat layer of the blood When similar areas were excised from the site of challenge it was found that skin from the control animal contained considerably more radioactivity per milligram than that from sensitized animals Although no constant differences in the amount of radioactivity present in the regional inguinal lymph nodes nor in the spleen of control and sensitized animals were found the buffy coat of sensitized animals contained more radioactivity per milligram than that of control animals No consistent differences were found in the white blood cell counts of sensitized and control guinea pigs Little or no radioactivity was found in the red blood cells and liver of any of the animals The radioactivity in the serum was somewhat higher and there was no difference between sensitized and control animals

The lesser amount of radioactivity found in the skin of sensitized guinea pigs might result from (1) more rapid loss of radioactivity externally as a result of a more successful effort by the sensitized animal to cast off the allergen from the site of challenge (2) an increased rate of removal of the radioactively tagged allergen internally achieved by the increased vascular lymph and other fluid flow to the site of challenge in the sensitized animal or (3) more rapid removal of the allergen or its degradation products in the

(3) J I t Derma 31 97 10 A — t 1958

actually handle them have not been alerted and therefore do not take adequate precautions Skin contact should be prevented by good plant housekeeping during the addition and processing of these agents Epoxy resins should be handled only in well ventilated areas although this is not always practicable Repeated instruction should be given to workers to avoid direct contact with any components used in processing Workers should be warned to wash off immediately any splatters or spilled material that may come in contact with the skin

► [As with acrylic resins the more highly polymerized the epoxy resins the lower the incidence of dermatitis Here is another of the increasing number of agents which are responsible for the rise in the incidence of primary irritant and allergic contact dermatitis among workers With the advances of science in industry this incidence is likely to continue to increase It is unfortunate that the advances in our understanding and prophylaxis of the resulting eruptions have not kept pace with the industrial progress —Eds]

Sensitizing Structure in Epoxy Resin L Edward Gaul (Evansville Ind) reports an instance of glue dermatitis traced to epoxy resin The hardener used was phthalic anhydride Patch tests were performed with 1% concentrations of the components in olive oil The patient was sensitive to a sample of air dried resin but not to heat cured resin

The epoxy group was not the sensitizer in this case Heat curing apparently alters the structure of the resin sufficiently to render innocuous the sensitizing group Apparently bisphenol A carried the allergenic portion of the resin A dilution test was positive in 24 hours to a concentration of 0 001% of the resin

The most important finding is the reaction to the air dried resin The patient may have had the sensitizing exposure either because the foreman at the plant added an insufficient amount of hardener or because the substance did not cure long enough In any event the sample was highly allergenic This observation suggests a need for awareness of the possibility of epoxy resin sensitization from diverse and unsuspected source

► [In these days and times the practitioner must be constantly alert to unsuspected and hidden sources of substances which potentially cause allergic or other reactions e.g the epoxy resins in glue antibiotics in fish fowl and milk hormones in capons etc —Eds]

(7) J Invest Dermat 29 311 313 November 19

ried to the organ by way of different groups of lymph nodes The authors had shown before that sensitization does not subside when the regional lymph nodes are removed after sensitization has been established This would suggest that these lymph nodes are not the only producers of antibodies Further studies should reveal the nature of the agent which is carried on from the regional lymph nodes centripetally and to determine the organs which besides the regional lymph node produce antibodies and preserve sensitization

Interference Phenomenon in Allergic Contact Dermatitis William I Epstein and Albert M Kligman[3] (Univ of Pennsylvania) observed that the simultaneous application of two contact allergens of unequal sensitizing capacity did not result in the expected incidences of sensitization the weaker allergen was blocked Original observations of this interference phenomenon were made with two highly potent contact allergens 2 4 dinitrochlorobenzene and paranitrosodimethyl aniline The frequency of sensitization to varying concentrations of each was worked out over several years in healthy adult Negro males Sensitization rates were within the expected range when the allergens were applied simultaneously to separate sites so long as the concentrations were alike or nearly so Simultaneous application of unequal concentrations to separate sites however gave frequency values for the weaker allergen (paranitrosodimethyl aniline) decidedly less than expected

Further investigation using allergens of varying concentration and potency established that only potent contact sensitizers can exert interference Stronger allergens can interfere with weaker ones but not vice versa The interfering allergen must be used at concentrations which give maximal rate of sensitization whereas the allergenic strength of the agent to be blocked must be considerably weaker In general interference seems to be an instance of competitive inhibition The stronger allergen pre empts the antibody synthesizing mechanism so that the claims of the weaker allergen cannot be satisfied The blocking effect lasts about 2 weeks after application of the interfering allergen

► [These investigations reveal data which strongly suggest the existence of an interference phenomenon However before this can be accepted as a totally original contribution it will have to be done As was pointed out by Eisen

[3] J I [illegible] Dermat 31 103-108 August 1958

sensitized animal resulting from processes associated with allergic sensitization

There is increasing evidence that the white blood cells in particular the mononuclear cells play an important role in the mechanism of allergic eczematous contact dermatitis. Demonstration of a higher level of radioactivity in the buffy coat of the sensitized guinea pig than in its other blood cells or serum indicates that the cells of the buffy coat carry at least part of the responsible allergen and suggests that they are in some way associated with the allergic process. This finding does not necessarily prove or disprove the presence or absence of an antibody to the responsible allergen.

► [No consistent changes in the white blood cell count in sensitized animals were observed during the first 12 hours after challenge. Seeberg (Acta dermat venereol 33 359 1953) had found an increase in the number of granulocytes in the blood 4-7 hours after challenge with the allergen DNCB. Polak (Arch klin u exper Dermat 201 124 1955) noted a relative increase in mononuclear cells and a relative decrease in polymorphonuclear cells between the 2d and 3d day after the sensitizing exposure, i.e. before the animals became hypersensitive.—Eds.]

Influence of Calmette Guerin Bacillus Infection on Dinitrochlorobenzene (DNCB) Contact Eczema of Guinea Pig is discussed by J. R. Frey and P. Wenk[4] (Basel). According to present day knowledge the changed reactivity of the entire skin after sensitization with DNCB is due to an antibody like principle. The authors found that sensitization of the guinea pig skin with DNCB was potentiated by simultaneous intracutaneous inoculation with Calmette Guerin bacillus if both antigens were given simultaneously and in the same skin area so that they reached the same group of regional lymph nodes. When the antigens were applied to separate skin areas so that each reached a different lymph node group potentiation was absent or minimal.

Contact eczema according to current theories depends on the development of specific antibodies and an increase in the antibodies must be assumed as a basis for potentiation. Since the authors' observations indicated that this potentiation takes place in the regional lymph nodes it may be assumed that antibodies are produced in these lymph nodes. If the source of antibodies were found to be exclusively some organ situated deeper than the regional lymph nodes potentiation would also take place when the antigens are car

(4) D[illegible] [illegible] 11 1 4 164 September 1 58

ried to the organ by way of different groups of lymph nodes. The authors had shown before that sensitization does not subside when the regional lymph nodes are removed after sensitization has been established. This would suggest that these lymph nodes are not the only producers of antibodies. Further studies should reveal the nature of the agent which is carried on from the regional lymph nodes centripetally and to determine the organs which besides the regional lymph nodes produce antibodies and preserve sensitization.

Interference Phenomenon in Allergic Contact Dermatitis. William L. Epstein and Albert M. Kligman[5] (Univ. of Pennsylvania) observed that the simultaneous application of two contact allergens of unequal sensitizing capacity did not result in the expected incidences of sensitization; the weaker allergen was blocked. Original observations of this interference phenomenon were made with two highly potent contact allergens, 2,4-dinitrochlorobenzene and paranitrosodimethyl aniline. The frequency of sensitization to varying concentrations of each was worked out over several years in healthy adult Negro males. Sensitization rates were within the expected range when the allergens were applied simultaneously to separate sites so long as the concentrations were alike or nearly so. Simultaneous application of unequal concentration to separate sites, however, gave frequency values for the weaker allergen (paranitrosodimethyl aniline) decidedly less than expected.

Further investigation using allergens of varying concentration and potency established that only potent contact sensitizers can exert interference. Stronger allergens can interfere with weaker ones but not vice versa. The interfering allergen must be used at concentrations which give maximal rates of sensitization, whereas the allergenic strength of the agent to be blocked must be considerably weaker. In general, interference seems to be an instance of competitive inhibition. The stronger allergen pre-empts the antibody-synthesizing mechanism so that the claims of the weaker allergen cannot be satisfied. The blocking effect lasts about 2 weeks after application of the interfering allergen.

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[5] J. Invest. Derma. 31:103-108, August, 1958.

and Sulzberger in the discussion to this paper the experimental method used does not rule out a nonimmunologic phenomenon Also the role of the *site* of application of the allergens is difficult to assess at this time The results of Frey and Wenk (see preceding article) for example clearly show that if two allergens are applied to sites of application which drain into the same regional lymph nodes this may have a different effect on the degree and incidence of sensitization as compared with application of two allergens to sites draining into different lymph nodes —Ed]

Histopathology of Contact Eczema with Reference to Sweat Retention D I McCallum[6] studied serial sections of 45 biopsy specimens from 24 patients with eczema The sweat ducts in the dermis and rete mucosum appeared to be



Fig 5 (left) —Part of sweat duct on right of vesicle and intact ampulla
Fig 6 (right) —Break in lower layers of stratum corneum around which leukocytes abound Stratum corneum in this area shows parakeratosis Sectioned sweat duct is at base of vesicle on right and superficial to it is extension of spherical vesicle into adjacent middermis
(Courtesy of McCallum D I Tr St John's Hosp Dermat Soc pp 58 Winter 1957)

resistant to the stresses caused by the eczema reaction They were usually displaced to one side of the vesicle (Figs 5 and 6) In a few instances they penetrated the vesicle without rupture In acute or long standing reactions they appeared to be elongated and compressed between the closely packed vesicles

At the greatest diameter of the vesicle the layer of stratum corneum lying immediately above the rete mucosum was frequently ruptured and its free margins were inverted into

(6) Tr St John's Hosp Dermat Soc pp 58 Winter 195

the vesicle cavity The rupture of the stratum corneum occurred at or close to the point at which the sweat duct entered the stratum corneum and was close to the ampulla of the duct (Fig 6) Frequent rupture of the sweat duct at the lower level of the stratum corneum in acute conditions could explain the sweat retention in some of these cases It would also explain the deleterious effect of sweating in these conditions When eczema vesiculation is severe enough to rupture the lower layers of the stratum corneum in the vicinity of the ampulla of the sweat duct stimulation of the gland could cause extravasation of its secretion into the tissues

In acute contact eczema degeneration of the epidermal cells of hair follicles was observed with lymphocytic infiltration around and within the follicle The infiltration was most pronounced in the upper epidermis just under the stratum corneum In some cases eczema vesicles occurred in the hair follicle The findings suggest that in cases of contact eczema the allergen gains entry into the skin by the skin appendages In both epidermis and dermis this produces changes which ultimately result in vesiculation The changes in the epidermis are essentially destructive those in the dermis are exudative

► [These findings in contact dermatitis are quite similar to those described in dyshidrotic and vesicular eruptions of the palms and soles by Herrmann *et al* (this YEAR BOOK p 277) —Eds]

Subungual Hemorrhage in Pan Washers Preliminary Report Peter I Long Jr[7] (Dayton O) reports 3 cases of subungual hemorrhage in pan washers at the Veterans Administration Center The 3 patients used heavy rubber gloves while working Other pan washers wore no gloves or only light cotton gloves to protect the hands from steel wool During the interval between discovery of the first and third patient the type of cleansing agent used for washing pans was changed from a powdered to a liquid detergent During the washing process each patient accumulated 50 175 cc washing solution in the rubber gloves The pH of the solution in the sinks was 7 1 10 0 whereas that in the gloves was 5 2 6 7

Only men who had been pan washers for a short time had subungual hemorrhages The fact that they were not accustomed to this type of labor may be an important factor in the cause However it is unlikely that the lesions were due to

(7) J A M A 168 122 12 7 N 1 19 8

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(6) Tr St John s Hosp Dermat Soc pp 5 8 W t r 195

rate of 3.3% was obtained for small plants in the chemical and allied products industry. This was the highest rate in any size group in any industry category. Little seasonal variation in incidence of dermatitis was observed during the 6 months of the study. Of 173 cases of dermatitis presumably due to petroleum products, 119 (69%) were considered to be due to cutting oils. Incidence of dermatitis due to cutting oils was 0.22% for all workers and 0.32% for production workers.

The authors conclude that with about 16,000,000 employees in the manufacturing industries, it might be expected on the basis of these figures that 128,000 occupational dermatitis cases would occur in the course of a year throughout the country. About 60,000 of these would be due to petroleum products, cutting compounds accounting for about 41,000.

Dermatitis. Report on 5½ Year Experience of an Ammunition Plant is presented by Arthur L. Knight[8] (Rochester, N.Y.). During the survey period there was a steady drop in the dermatitis rate from 75 cases/1,000,000 man hours in 1951 to 17 cases in 1957. The yearly occupational dermatitis rate dropped from 49 to 8 cases/1,000,000 man hours. The decline in dermatitis was similar to the decline in over-all occupational sickness and accident rate. Knight discusses factors believed to be important in the reduction of the occupational disease rate.

The standards of pre-employment examinations were raised during the survey period. Employees with a history of dermatitis were not hired for toxic operations. Those with a history of hay fever or asthma were restricted from working in most toxic areas. The physical examination was broadened to include a complete skin survey. No one with an active skin lesion such as acne, eczema, dermatophytosis or psoriasis was hired for work in a manufacturing area. Annual examinations including skin surveys were carried out. If a skin disease was detected, the employee was kept from toxic exposure and was treated. Employees in toxic areas were given monthly medical examinations. These helped insure that dermatitis did not go undetected and untreated. Employees were constantly asked to seek early treatment of skin eruption. An effort was made not to overtreat any dermatitis.

[8] A.M.A. Arch. Ind. Health 18:1-16, August 1958.

pure trauma because they probably would be more common if this were the case. The change to the acid side in the pH of the detergent solution trapped in the gloves may have caused breakdown of the detergent with subsequent release of a more irritating substance in the form of a sulfonic acid. This possibility is being investigated.

In the 3 patients, subungual hemorrhages subsided and the lesions completely cleared after the patients were removed from their jobs. Prompt recognition of the lesions and elimination of the offending agent is necessary to prevent extensive nail bed damage.

► [The illustrations in this article demonstrate that these subungual hemorrhages are much more massive than the characteristic splinter-like hemorrhages seen associated with subacute bacterial endocarditis and trichinosis.—Eds.]

Dermatitis in Industry: Pilot Study with Special Reference to Oils as Causative Factor is reported by Daniel C. Braun and Kosedith Sitgreaves[8] (Industrial Hygiene Found., Pittsburgh). Records were obtained of every patient with dermatitis reporting to the dispensaries of 36 companies with 103,586 employees. The companies were located in 5 geographic areas and represented 8 industrial categories. The study was carried out during 6 months. There were fewer than 500 employees in 13 companies, 500-1,000 in 7, 1,000-10,000 in 13, 10,000-20,000 in 2 and over 20,000 in 1. Two thirds of all employees covered were in the fabricated metal products industry. All but 1 plant provided exposure to solvents, all but 2 to grease, all but 4 to cutting oils and to chemicals such as acids and alkalis, and all provided some possibility of contact with petroleum products.

For all employees, the rate for occupational dermatitis was 0.8% adjusted on an annual basis. The rate for dermatitis due or probably due to oil was 0.3%. When the reported cases were related to production workers only, who were in effect the exposed group, the incidence rose to 1.2% for occupational dermatitis and to 0.5% for dermatitis due to oils and greases. The rates for female production workers were roughly twice the corresponding rates for males. Incidence rates could not be correlated with race and complexion in this study. In general, plants with less than 1,000 employees reported few cases of occupational dermatitis. However, a

(8) A.M.A. Arch. Indust. Health 17:39-2, Apr. 1958.

soiled hands or on the inner thighs due to clenching the shoes between them

The cement is composed of (1) synthetic rubber Neoprene AC (2) phenolformaldehyde resin CKR 1634 (Union Carbide) composed of para tertiary butylphenol formaldehyde and an unknown catalyst and (3) zinc and magnesium oxides toluene ethylacetate and benzene Ten patients patch tested with these substances had reactions to the resin and to para tertiary butylphenol Two also had reactions to formaldehyde

Several other commonly used shoe adhesives contain para tertiary butylphenol (or a closely related substance) Several patients sensitized to Saba Select have had recurrences of dermatitis when working with other adhesives

The author proposes several preventive measures All gluing should be done in a separate part of the shop and at a particular time during the day Gloves aprons and tools should be used only for this work The soles to be brushed should be held with a fork in slots in the work bench A glove should be worn on the right hand while brushing on the glue and on the left hand while the sole is held in place during hammering The working surface should be covered with a sheet of paper which is discarded at the close of work Splashes of adhesive on the skin should be removed with ethyl acetate followed by soap and water

► [It would be surprising if allergic contact dermatitis did not occur *occasionally* in wearers of shoes made with adhesives containing para tertiary butylphenol —Eds]

Problem of Prolonged and Recurrent Industrial Dermatitis is evaluated by the Committee on Occupational Dermatoses Council on Industrial Health American Medical Association[2] The chief reasons for failure to bring about cure in some patients suspected of having occupational dermatoses are listed in the order of their importance

1 Incorrect dermatologic diagnosis Such diseases as nummular eczema infectious eczematoid dermatitis dyshidrosis superficial fungous infection lichen planus and psoriasis are frequently misdiagnosed as occupational A carefully detailed history is most important in establishing a diagnosis of occupational contact dermatitis Patch tests may be valuable diagnostic aids but only if used properly

(2) J A M A 168 516-520 Oct 4 1958

Lectures posters and safety talks were used in the directed ucation of employees

A campaign was undertaken to supply adequate rest rooms of high standard Each rest room was inspected every 2-4 weeks A high standard of cleanliness and housekeeping in work areas was developed Complete change of clothing was furnished daily to workers in toxic areas Other workers on dirty jobs were furnished coveralls Most employees were given the facilities and opportunity for showering after work Indicator soap was used in TNT toxic areas Investigation and control of dust fumes solvents gases noise heat humidity and nuisances became routine If possible the environment was controlled and toxic contamination eliminated, so that protective equipment could be discontinued Consequently during the survey period all but two respirators were removed Fewer protective gloves were required Protective creams were discontinued Automatic machines conveyor belts drag lines etc, were gradually introduced to reduce employee exposure to toxic hazards

► [This article points out that careful industrial engineering together with training for proper habits of cleanliness of the employees and the selection of workers for specific jobs can indeed lower the incidence of occupational dermatoses as well as other occupational illnesses and accidents However the case history and results of an examination of the skin for dermatose require careful evaluation so as not to exclude from work individuals whose cutaneous lesions would in no way introduce a hazard to themselves when employed for selected forms of work —Eds]

Occupational Eczema Due to Para Tertiary Butylphenol in Shoe Adhesive A few months after introduction of a new type of shoe adhesive K E Malten[1] (Leiden The Netherland) observed several cases of occupational dermatitis The adhesive Saba Select is used to bind the outer and inner soles The outer sole is held between the fingers of the left hand and the adhesive is applied with a brush in the right hand then it is allowed to dry for 30 minutes The outer sole is placed on the inner and the soles are hammered together The prevailing sites of dermatitis have been the finger tips and finger webs of the left hand the proximal third of the left palm and occasionally the fingers of the right hand and the volar aspects of both wrists Lesions have also been observed on the face and neck due to direct contact with the

(1) Dermatol g a 117 103 109 August 1 58

presence of fungous disease and presence of a constitutional skin disease or atopic background

► [The high incidence of industrial dermatitis together with the continued introduction of new potential allergenic substances increases the need for careful planning and prophylactic measures in industry in the attempt to avoid primary sensitizations as well as cross sensitizations—Eds]

Prognosis in Industrial Dermatitis F F Hellier[3] (Leeds England) reports the findings in a follow up by means of a questionnaire of 124 working persons who had been examined 4-6 years previously because of industrial dermatitis Further attacks of dermatitis had been experienced by 95 patients (80% of the men and 67% of the women) Earning capacity had diminished because of the original attack of dermatitis in 73 instances (59%) In persons over age 50 earning capacity was reduced in 68% in those under 50 earning capacity was lower in 53% Among patients whose original dermatitis occurred as a result of primary irritants (soap detergent friction sweating etc) only 8 of 59 (14%) had *no* further trouble whereas of those who had reacted to sensitizing agents 21 of 65 (32%) remained clear

Only 29 persons (23%) were still in the work they were doing when dermatitis first occurred Six patients had *never* been able to return to work of any kind Of the 29 who did not change work 22 (76%) had further attacks of 89 who changed work 67 (75%) had subsequent dermatitis Only 7 persons in the whole group were able to *continue at their old* work without dermatitis Of these 4 had made some modification of the conditions of their work (a bath attendant used a different method of cleaning a joiner avoided glue a lamp fitter wore gloves and an engineer used a heavy barrier cream) The other 3 were a baker an office cleaner and a coal miner about whom no detailed information was available

The findings suggest that complete immunity from further attack of dermatitis rarely comes except with a change of working conditions It seems therefore that a worker who is truly sensitized should be removed from the offending agent as soon as possible However a change of work does not guarantee freedom from trouble particularly for those reacting to primary irritants

► [This study reveals several important facts Among them *is* that the chance of permanent clearing are more than twice as great in industrial dermatitis due to allergen sensitizers than in cases due to primary irri-

(3) Brit M J 1 196-198 Jan 25 1958

2 Failure to establish cause Discovery of the cause may be especially difficult in workers who go from job to job in the plant

3 Failure to eliminate the cause after correct discovery and diagnosis After the skin heals some workers are put back on the same job by supervisory personnel Others are *reluctant to give up skilled jobs for those with less pay* and continue working with hazardous materials despite medical advice A complete change of job in the same department sometimes fails because the air tools benches and doorknobs may be contaminated with the chemicals responsible for the dermatitis

4 Improper medication This may be a home remedy with *which the patient experiments or the wrong type prescribed* by the physician

5 Development of secondary infections nummular eczema or dyshidrosis When these complications exist bland therapy usually effective in uncomplicated dermatitis fails to achieve satisfactory results

6 Poor facilities and improper cleansing agents Patient *with occupational dermatitis are prone to exacerbation* from the use of poor grade alkaline soap and organic fat solvent e g naphtha kerosene and gasoline for cleansing the hands

7 Placing dermatitis prone persons on hazardous new jobs

8 Cross sensitivity Patients may develop dermatitis as a result of exposure to one substance in the plant and have a recurrence due to contact with a structurally related chemical either on a new job or in nonoccupational pursuits

9 Development of multiple reactivities The cause of the phenomenon is not known but it must be considered as a possible reason *for persistent dermatitis in a patient who has* been removed from contact with the specific allergen or irritant

10 Malingering This factor is often suspected but is difficult to prove Rehabilitation and proper job placement with better compensation laws should do much to prevent malingering

Other less *important factor that may be responsible* for failure to bring about cure in individual cases of occupational dermatitis are active focus of infection elsewhere

eczema having scattered and grouped pruritic vesicles usually with surrounding erythema suggest dermatitis herpetiformis With formation of eczematoid orbicular lesions there is a similarity to disseminated nummular eczema At the multiformity stage a clinical parallel to exudative discoid and lichenoid chronic dermato is is apparent In the final stages of a classic cycle of generalized autogenous eczema dermatitis exfoliativa or generalized neurodermatitis are suggested by the clinical picture

Among the 60 patients an allergic or atopic diathesis was noted in a significant number and most related underlying tensions and emotional difficulties Such findings are common in the dermatoses which generalized autogenous eczema resembles Differentiation of these diseases from generalized autogenous eczema rests mainly on the precipitating local dermatitis and close observation of the course of the eruption

A simple cellular focal vascular reaction was observed in most microscopic sections of generalized autogenous eczema studied and appeared closely related to the neurodermatitic reaction Complicating secondary histologic features may be present depending on the biopsy site age of the lesion examined and exogenous factors such as secondary infection rubbing and scratching and local medication

These observations suggest that neurodermatitis nummular eczema exudative discoid and lichenoid chronic dermato i dermatitis herpetiformis and generalized autogenous eczema belong to the same group of diseases

► [In the experimental animal it has not been possible to engender sensi t at on to autologous skin using the same technics which did succeed in producing sen tization to autologous brain testicular and lens substance etc (see the following *article*) Since the basic principle of autosensitization to skin is not as *yet firmly formulated* it seems unwise to attempt to apply this conc pt in such *well established* utaneous entities as atopic d rmatit s dermatitis herpet forms and so forth.—Eds]

Failure to Sensitize to Autologous Skin is reported by Stanley A Rosenthal Rudolf L Baer and Blanka Hagel[6] (New York Univ Post Grad Med School and Skin and Cancer Unit)

METHOD —Emul ions of autologous skin were prepared using sampl s of skin removed from clipped and shaved flanks of guinea pigs

(6) P oc Soc Expe P 1 & Med 97 279 81 F b ry 1958

tants This is probably explained by the greater opportunity for strict avoidance of known specific sensitizers than of the ill defined category of primary irritants An incidence of 68% recurrences in allergic industrial dermatitis and of 86% recurrences in primary irritant industrial dermatitis is a rather sad commentary on preventive management of these common eruptions —Eds]

Thrombocyte Index after Injection of Staphylococcus Vaccine and Tuberculin in Man A fall in the thrombocyte index on supply of antigen is a common feature of allergy to foods and medicaments This phenomenon is also observed within a few minutes of administration of pollen extract in human subjects hypersensitive to pollen In anaphylactic shock in animals and in eczema types of reactions there is also a thrombocyte fall Åke Nilzen[4] (Karolinska Hosp Stockholm) made thrombocyte counts every 15 minutes for 90 minutes after injection of staphylococcus vaccine (about 90 000 000 organisms) staphylococcus toxoid (0 3 ml of 1 10 dilution) and tuberculin (0 003 mg)

A definite fall of the thrombocytes was observed after subcutaneous administration of staphylococcus vaccine and toxoid in patients who showed a positive skin reaction to the allergen There was no appreciable difference in the thrombocyte fall for subjects with immediate or delayed response A fall in thrombocyte count was also observed after injection of tuberculin in patients with positive reactions to skin tests with this material Though some of the controls (with negative skin reactions to the allergen) displayed a reduction in thrombocyte values, there was a clear correlation between the fall of thrombocytes and the positive skin response A 20% thrombocyte fall was regarded as significant Results indicate that the fall may be recorded if samples are taken 30 and 75 minutes after injection of the antigen

► [These studies confirm the results of Storck Hoigne and Koller and others Apparently the fall in thrombocyte count occurs on exposure to the allergen in many different forms of allergic sensitization —Eds]

Dynamics of Autosensitization Dermatitis Clinical and Microscopic Concept of Autoeczematization on the basis of a study of 60 cases is presented by Alexander W Young, Jr[5] (St Luke s Hosp New York) The usual stages of generalized autogenous eczema are the vesicular organizing confluent (spreading) multiform (diffuse) and resolving (generalized) The earlier stages of generalized autogenous

(4) Acta dermat venereol 38 332 372 1958
(5) A M A Arch Dermat 77 495 50 May 19 8

which begins after age 30 Although about half the patients with constitutional neurodermatitis form reagins their etiologic significance is questionable

It was found that persons with constitutional neurodermatitis without asthma and without allergic rhinitis form reagins less frequently than do those with asthma or allergic rhinitis

Studies in 112 families of patients with constitutional neurodermatitis and 235 families of patients with bronchial asthma and rhinitis pollinosa revealed that the individual diseases frequently involve the site which is the commonest for that disease in the family

Phenotypic Familial Pathologic Behavior of Atopies (Constitutional Neurodermatitis Bronchial Asthma Allergic Rhinitis) U W Schnyder and W Klunker[8] (Univ Skin Clinic Zurich) reviewed the families of 347 unselected patients with atopic diseases There were 112 patients with constitutional neurodermatitis 86 of whom had also respiratory involvement and 235 with bronchial asthma and rhinitis pollinosa

Among the families of the 112 patients with constitutional neurodermatitis 41% of the F 1 and P 2 generations on the maternal and paternal side were not affected by asthma rhinitis or neurodermatitis Of 26 patients with neurodermatitis without asthma or rhinitis 6 (23%) had ancestors with neurodermatitis only In 2 of the 26 families neurodermatitis was found on one side of the family and asthma or rhinitis on the other side

Among the 86 patients with neurodermatitis who also had respiratory affections if a hereditary trait was present the ancestors had alternating or in combination manifestations of asthma rhinitis or neurodermatitis (so called polyphenia)

In about a third of the 235 patients with asthma or rhinitis pollinosa the allergy manifested itself in 3 generations always only as asthma or only as allergic rhinitis while in two third the signs of asthma or rhinitis appeared in the ancestors either singly or in combination In 11 of the 235 families neurodermatitis was found among the ancestors

It was concluded that bronchial asthma and allergic rhinitis on the one hand and constitutional neurodermatitis on the

(8) H t rt 8 510 511 N mbe 19 2

Skin was weighed to the nearest 0 1 Gm minced with scissors and added to 4 volumes of sterile saline or staphylococcus toxin diluted 1 5 with saline This crude skin suspension was fragmented in a high speed homogenizer The resulting skin broth was taken up through a 20 or 21 gauge needle and emulsified in a syringe with 2 volumes of a mixture of Bayol F and Arlacel A containing 1 mg of killed dried tubercle bacilli/ml The ratio of Bayol F to Arlacel A was either 8½ 1½ or 2 1 Thus each milliliter of skin adjuvant emulsion contained approximately 67 mg of skin Test animals received injections of their autologous skin emulsion with adjuvants whereas control animals were given an emulsion of saline or staphylococcus toxin diluted 1 5 with saline with adjuvants

Eighty nine guinea pigs were given injections intracutaneously intramuscularly or intraperitoneally with autologous skin emulsion and 38 with control emulsion Animals received autografts 28 64 days after the first injection of skin or control emulsion There was no significant difference in the percentages of skin autografts accepted and rejected between the animals pretreated with an emulsion of their own skin and control animals Irritancy tests such as scraping and burning the skin did not produce different results in the two groups Thus neither the autograft experiments nor the irritation tests produced evidence indicating that sensitization to autologous skin had taken place after intracutaneous intramuscular or intraperitoneal injections of autologous skin and adjuvants

Allergic and Familial Background of Atopies is discussed by U W Schnyder (Univ Skin Clinic Zurich) Constitutional neurodermatitis (Besnier s prurigo atopic dermatitis), together with bronchial asthma and allergic rhinitis has been considered as an atopic or familial dispositional allergic disease However atopic allergy has a different etiologic significance in the three diseases

In the various forms of allergic rhinitis sensitization against *pollen grasses feathers* various animal hairs and other inhalant allergens has primary etiologic significance The clinical signs of allergic rhinitis usually appear within a few minutes after exposure Of the various forms of bronchial asthma only hay fever and baker s asthma behave as does allergic rhinitis In about 40% of all asthmatics no atopic hypersensitivity can be demonstrated This holds especially for patients with so called intrinsic asthma

(7) *Dermatologica* 116 83 86 April Ma 1958

onset of hay fever and asthma direct hypnotic suggestions were made for the first time about her symptoms She was told that she would have no hay fever or asthma During the ensuing season she was entirely well for the first time Weekly hypnotic treatment was continued during this period and she was skin tested on the left arm after each treatment Sensitivity reactions gradually decreased to zero during 7 weeks However when she was unexpectedly tested on the left leg (a site not previously used for testing) skin te ts were again markedly positive She was then told while in hypnotic trance that the skin would henceforth be unresponsive on all parts of her body After this trance skin tests were negative on both arms and both legs With the patient consistently free from asthma hay fever and any skin responses when tested with known allergens a passive transfer test was performed and a reaction was obtained with 2 of the 3 known allergens

By direct suggestion under hypnosis an overriding psychic system of control was established in this patient which could not only keep her well but could inhibit selectively the allergic reaction in different parts of the body Although presumably central in origin this control system because of its powers of selectivity might be assumed to act peripherally

In this case laboratory control produced results which support the general clinical observation that three factors may be involved in the etiology of asthma and hay fever foreign proteins sensitized tissues and a psychogenic factor In this patient at least the psychogenic element was shown to be the most powerful possibly explaining why psychologic treatment in the form of suggestion under hypnosis provided complete relief from symptoms whereas other methods of treatment were only partly successful

► [A most interesting report of the power of strong hypnotic suggestion on disease and on the reactivity of the skin to urticariogenic allergens The authors conclusions that the psychogenic element was the most powerful etiologic factor in their patient because of her favorable response to hypnotic suggestion seems unwarranted Would they have concluded that the adrenal glands are the most important etiologic factor if they had suppressed the hay fever and asthma in this patient by giving large doses of corticosteroids or if they had suppressed the skin test reactions to the grasses trees and spring flowers by the prior administration of epinephrine? —Eds]

Observations on Delayed Blanch Phenomenon in Atopic Subjects Michael J Davis and James C Lawler[2] (Walter Reed Army Med Center) studied the superficial vascular response of 15 atopic subjects to locally applied acetylcholine by direct observation of the vessels with a capillary mi

[2] J I est Derm t 30 127 132 M h 1958

other do not behave similarly in their phenotype Patients with neurodermatitis without involvement of the respiratory tract usually carry only the hereditary trait of neurodermatitis Neurodermatitis patients with conditions of the respiratory tract usually come from families with manifestations of asthma, rhinitis or neurodermatitis So called poly phenotypic' ancestral lines are rare among patients with atopic diseases They are mostly found among patients with constitutional neurodermatitis and asthma and/or rhinitis

Pulmonary Function in Endogenous Eczema According to E Lutz and G W Korting[9] (Univ Skin Clinic, Tubingen), the concomitant as well as the alternating behavior of endogenous eczema and bronchial asthma point to the existence of a similar diathesis in both The authors studied pulmonary function (respiratory rate vital capacity, respiratory volume per minute etc) in 25 patients with endogenous eczema and in 20 controls of about the same age and with similarly extensive skin affections of various cause before and after use of Aludrine an antiasthmatic compound Latent susceptibility for asthma (pulmonary dystonia) was found in 60% of the patients and in 5% of the controls

In 8 of 12 patients who had endogenous eczema but no individual or familial asthmatic trait the pulmonary function studies did not reveal pulmonary dystonia This suggests hereditary familial differences in patients with endogenous eczema implying that there are families with endogenous eczema with or without involvement of the respiratory tract

► [These findings fit in with those of Schnyder (see 2 preceding articles) that there are two distinct groups of atopic dermatitis patients namely those with a hereditary trait for atopic dermatitis and those with a hereditary trait for atopic dermatitis *and* respiratory allergies —Eds]

Allergic Skin Responses Abolished under Treatment of Asthma and Hay Fever by Hypnosis A A Mason and Stephen Black[1] (London) report a case

Woman 27 had had incapacitating hay fever and asthma from May to July each year for 12 years One year previously she had some relief from symptoms after hyposensitization but remained sensitive to 3 known allergens (extracts of grasses trees and spring flowers) Because of the limited benefit obtained from hyposensitization she refused further treatment of this kind and was referred for hypnosis

Before the expected onset of symptoms in May she was given weekly hypnotic treatments for 2 months One week before the expected

(9) Arch klin u exper Dermat 205 597 604 1958
(1) Lancet 1 877 880 Apr 26 1958

and Charles F Code[3] (Mayo Clinic and Found) White dermographism is the vasoconstriction of minute cutaneous vessels and is seen after light stroking of normal skin The reaction persisted with both light and heavy stroking in chronic inflammation of the skin The reaction occurred in chronic infiltrative conditions such as atopic dermatitis disseminated neurodermatitis psoriatic erythroderma mycosis fungoides and lymphomatous erythroderma and was not specific for atopic dermatitis The white reaction was not seen in acute inflammatory conditions Patients with superficial dermatoses such as parapsoriasis pityriasis rosea and superficial localized psoriasis either did not exhibit the reaction or showed it only slightly These patients had a red line with a flare or a white halo Several patients with atopic dermatitis or generalized psoriasis showed loss of white dermographism when the cutaneous lesions disappeared

In attempting to inhibit the white reaction various agents were injected that are known to block the action of chemicals that occur naturally in the skin and cause vascular responses Diphenhydramine (Benadryl®) hydrochloride was used to inhibit the action of histamine phentolamine (Regitine®) hydrochloride to inhibit the action of adrenergic compounds and atropine to inhibit cholinergic compounds procaine was used to produce localized anesthesia None of these agents injected intradermally inhibited the appearance of the white reaction produced by stroking

The results seem to imply that white dermographism depends on mechanical stimulation of the skin which induces capillary constriction and apparently is independent of any chemical or nerve stimulus In chronic inflammation the skin capillaries apparently are altered by the inflammatory process and increased vascular tone results

[The vessels probably showed increased vascular tone as a result of chronic inflammation Alterations in vascular tone may well be the result [illegible] some locally altered biochemistry The question remains whether a chronically inflamed skin produces a chemical substance as yet unidentified which is activated to cause vasoconstriction following mechanical stimulation of the skin in the diseases noted —Eds]

II [illegible] tion of epinephrine and phentolamine (regitine®) action of acetylcholine and methacholine (mecholyl®) and delayed blanch were investigated by Reed and Kierland[4] Epi

(3) A.M.A. Arch. Derm. 91-96, January 1958
(4) Ibid. pp. 181-186, February 1958

croscope. The sites were prepared by repeated applications of cellulose tape until the keratin layer had been removed. At least 1 hour was then allowed to elapse before testing.

Capillaries in the areas of the acetylcholine induced wheal and delayed blanch reaction remained dilated though the areas turned pale grossly. There was increased accumulation of fluid in the wheal and about its periphery which accounted for the gross paleness. The local vasodilating effect of acetylcholine induces a temporary increase in capillary permeability in and about the wheal with consequent leakage of fluid into the corium. The fluid leaking out of the capillaries to form a wheal displaces peripherally the tissue fluids present in the area. Since there is edema in the corium in atopic dermatitis more fluid is present to be displaced in wheal formation. This could partially explain the pale halo which is noticeable about acetylcholine induced wheals in atopic skin.

The presence of white pseudopods around the periphery of an acetylcholine wheal probably represents the effect of the agent which is being transported through lymphatics away from the injection site and is diffused out of the lymphatics to act on the blood vessels along them.

Hyaluronidase diminished the size of the wheal and its paleness when introduced into the skin with or before acetylcholine and the delayed blanch phenomenon did not occur presumably because the fluid was diffused more rapidly.

The delay in appearance of a pale zone around the acetylcholine wheal is consistent with the impression that displacement of fluid is involved in formation of the delayed blanch zone. Sweat retention may also contribute to the observed paleness in and about the wheal from acetylcholine possibly by causing maceration of the keratin layer.

► [The exact nature of white dermographism and delayed blanch phenomenon in atopic dermatitis remains to be elucidated. The finding of Davis and Lawler demonstrating vasodilatation and pericapillary edema formation contradict the generally held concept that these phenomena are due to vasoconstriction. The speed with which the blanching occurs in white dermographism perhaps would be explained more readily by vasoconstriction than by edema formation. Furthermore, if edema formation were the correct explanation one would expect that occasionally at least wheals or some other expression of edema would become clinically evident.—Eds.]

Vascular Reactions in Chronically Inflamed Skin.— *Mechanical stimuli to skin (inhibition of white dermographism)* was attempted by William B. Reed, Robert R. Kierland

tory processes the flare being masked partly or completely by the already dilated minute vessels of the skin

Injection of 48 80 into normal skin produced a strong flare Inflammation of the skin reduced the size of the flare the reduction paralleled the acuteness of the cutaneous disease The size of the wheal also was reduced in more inflammatory conditions the reduction was more pronounced with 48 80 than with histamine The weaker response to 48-80 may have resulted from two factors (1) The histamine released was removed almost immediately by the increased circulation in the skin (2) The amount of bound histamine available was reduced with less histamine being liberated by 48-80

The flare after an injection of histamine in patients with white dermographism can be reduced or abolished when the affected skin is rubbed before or after the injection Histamine induced pruritus may be reduced by stroking the skin and thus abolishing the flare response by producing vasoconstriction of the minute vessels of the skin With release o constriction pruritus returns

Monoethanolamine nicotinate an ester of nicotinic aci that has nicotinic acid activity did not have the paradoxica action of acetylcholine viz production of the delayed blanch when injected intradermally

► [Reed and co workers here have answered a question which many hav asked namely is white dermographism specific for atopic dermatitis While it is most commonly seen in atopic dermatitis it obviously also oc curs in other chronic inflammatory conditions

The fact that none of the pharmacologic agents tested inhibited whi dermographism might be explained by the fact that they do not interfe with direct mechanical stimulation of the capillaries or as proposed Da that white dermographism is not due to vasoconstriction Howeve diphenhydramine which decreases capillary permeability in addition blocking certain vascular response would have been expected to inte te with white dermographism if Davis theory is correct

Thus while white dermographism cannot be used as a pathognomo sign for atopic dermatitis the delayed blanch response described by Lob and Campbell apparently occurs only in atopic dermatitis and only in ffected areas —Eds]

Basophil Leukocytes in Urticaria Asthma and Ato Dermatitis Basophil leukocytes and tissue mast cells ha several characteristics in common Both stain metachrom ically with basic aniline dyes contain heparin or a hepar like substance and have a high content of histamine Wh

nephrine (0 1 ml of 1 10 000 and 1 100 000 dilutions) was injected into the skin of 11 patients with atopic dermatitis 4 with disseminated neurodermatitis 5 with psoriatic erythroderma and 3 with mycosis fungoides All patients showed immediate vasoconstriction after epinephrine injection though the size of the blanched zone was smaller in patients with more acute forms of dermatitis

Phentolamine, injected intradermally produced a small red injection wheal with an axon reflex no different from that following injection of isotonic saline solution When both phentolamine and epinephrine were injected intradermally the central portion of the injection wheal was red and was surrounded by a blanched zone produced by the epinephrine The red zone representing the antiadrenergic action of phentolamine slowly expanded engulfing the blanched portion A dose of 0 1 ml of 1 1000 phentolamine inhibited completely the effect of 0 1 ml of 1 10 000 epinephrine

The delayed blanch noted after intradermal injection of acetylcholine in atopic dermatitis was not found in the other inflammatory conditions studied nor was it present in older subjects with disseminated neurodermatitis This paradoxical reaction to acetylcholine did not occur in zones of normal skin in patients with atopic dermatitis The delayed blanch was inhibited in part or completely by intradermal injection of atropine but not by injection of phentolamine diphenhydramine or procaine This reaction to acetylcholine and other cholinergic drugs when present may be used to differentiate atopic dermatitis from similar inflammatory cutaneous diseases

III Action of histamine histamine releaser 48 80 and monoethanolamine nicotinate (nicamin®) were also studied by Reed Kierland and Code [5] Histamine (1 10 000 and 1 100 000) and the compound 48 80 (1 100 000 and 1 500 000) a potent histamine releaser were injected into normal skin and into the inflamed skin of patients with atopic dermatitis disseminated neurodermatitis psoriatic erythroderma and mycosis fungoides The size of the wheal produced by histamine was reduced in more acute conditions but was nearer normal in chronically inflamed and slightly erythematous skin The size of the flare also was reduced in more acutely inflamma

(5) A M A Arch Dermat 77 63 68 March 1958

tory processes the flare being masked partly or completely by the already dilated minute vessels of the skin

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Basophil Leukocytes in Urticaria Asthma and Atopic Dermatitis Basophil leukocytes and tissue mast cells have several characteristics in common Both stain metachromatically with basic aniline dyes contain heparin or a heparin like substance and have a high content of histamine When

histamine is liberated from mast cells in experimental animals the animals may exhibit symptoms of anaphylactic shock Because of these findings Hans Rorsman[6] (Univ of Lund) studied the mast cells in the blood of persons with allergic disorders

Using a modification of the method of Moore and James basophil leukocytes were counted in 96 controls 22 patient with urticaria 20 with asthma and 30 with atopic dermatiti A marked decrease in the number of basophils was found in most cases of urticaria and in some cases a complete disappearance of these cells A few patients had normal count The average count in the control group was 44 8 ± 2 4 cells/cu mm and in cases of urticaria the average count was 8(±2 7 The average for asthmatics was 55 3 ±5 6 cell /cu mm blood and in atopic dermatitis 44 3 ± 4 6

The decrease in basophils in urticaria is probably the morphologic basis for the decrease in blood histamine that has been observed in this condition The author found a good correlation between the low histamine content in the blood of certain patients with urticaria and a low basophil count In patients with higher counts a greater concentration of histamine was found In 3 patients with cold urticaria a normal basophil count and normal histamine concentration were observed

The factors which determine whether a patient with urticaria has a normal or low basophil count have not been discovered A normal count has been noted in dermographism and emotional urticaria as well as cold urticaria In 3 patients with urticaria pigmentosa the basophil counts were 19 5 15 and 21 5 cells/cu mm respectively whereas in a fourth patient who was allergic to acetylsalicylic acid the count was 2

The basophil count usually return to normal during the first few days after an acute attack of urticaria but in some cases counts remain low for several weeks The mechanism causing a decrease in the basophil count in urticaria is not known Possibly the basophil leukocytes are destroyed in the blood stream or migrate into the reacting skin areas

► [Robert Bersani at the New York Skin and Cancer Unit has been able to confirm Rorsman's results in urticaria In atopic dermatitis he

(6) Acta allergol 12 05 08 1958

found lower basophil counts than Korsman although the number of atopic dermatitis patients studied thus far is too small to make these differences statistically significant. The results in atopic dermatitis also may depend on the severity and extent of cutaneous involvement. In allergic contact dermatitis Bersani encountered normal basophil counts.—Ed]

Results of Correlative Statistics in Over 2 000 Electrophoretic Determinations (According to Antweiler) in Neurodermitis Brocq (Atopic Eczema) and Other Eczemas are summarized by C M Hasselmann[7] (Univ of Erlangen) Neurodermitis Brocq is characterized by a papular shiny infiltrated coarsely patterned skin by chronic intermittent course with severe itching occasional lymphadenitis and frequent secondary pyoderma and by its typical localization in the elbows bends of the knees neck forehead around the eyebrows sacrum perianal region vulva and scrotum

To detect possible permanent biochemical changes characteristic of neurodermitis electrophoretic determinations were carried out on the serum of patients with neurodermitis and various forms of eczema The Antweiler method was used which proved to be more dependable and accurate than paper electrophoresis

As normal mean values those suggested by Wernsdorfer were considered albumin 58 8 ± 1 7 alpha globulin 9 4 ± 0 6 beta globulin 11 6 ± 0 6 gamma globulin 19 4 ± 0 4

Using the statistical formula

$$\frac{|\overline{X}_N - \overline{X}_F|}{\sqrt{\frac{\sigma_N}{N_N} + \frac{\sigma^2_F}{N_F}}}$$

neurodermitis patients showed significantly decreased albumin significantly increased gamma globulin and questionably increased beta globulin Similarly hypoalbuminemia and increased beta and gamma globulins were found in two groups of eczematous patients Significantly increased alpha globulins were found in one group of eczematous patients

The highest alpha globulin reading 24 4% was found in a woman with psoriatic erythroderma and the highest beta globulin 34 2% in a woman with latent syphilis and hepatitis The highest gamma globulin reading of 61 3% was seen in a man with chronic eczema and of 61 7% in a woman

(7) A h kl pe De mat 205 373 380 1957

with icterus during treatment for malaria The lowest albumin reading 21 2% was seen in a man with pemphigus

The combination of increased beta and gamma globulin is interpreted as the typical 'plasma syndrome of a diseased liver The apparent practical insignificance of these findings together with the obscurity surrounding the etiology of neurodermitis combined with the almost demonic" recurrences and clinical course, suggest correlation of the clinical appearance of the disease with the psychosomatic make up of the patient

► [The wealth of significant findings regarding atopic dermatitis which have been accumulated weighs heavily against the apparent practical insignificance of these electrophoretic findings While no *single* etiologic mechanism has been found (and while perhaps none exists) the knowledge available on atopic dermatitis surpasses that available for certain other common dermatoses (e g psoriasis lichen planus) by far The demoni recurrences of atopic dermatitis generally are readily amenable to treatment and when successfully treated appear to leave a patient with no more than the average amount of emotional problems

It is of interest in view of Haselmann s electrophoretic observations that Robert Good has reported that atopic dermatitis does occur among subjects with agammaglobulinemia —Eds]

Cholinergic Urticaria and Miliaria Maurice Garrett[8] (Univ College Hosp London) studied 2 cases of typical cholinergic urticaria The patients were young men who described attacks of small irritating wheals which occurred at embarrassing interview at dances or when playing football Hot weather always made the disease worse Whealing could be produced in both patients by warming the arm in water at 45 C for 20 minutes by an injection of pilocarpine or by exercise on a stationary bicycle One patient stated that he could not sweat and that the rash appeared when he was hot In both patients during whealing produced by heating copious sweating occurred from the axillae neck face groins and feet but only a little sweating on the trunk and thighs where lesions were most profuse The wheals consisted of papules, 2 3 mm in diameter dome shaped and pale pink and around them an intense flare spread over an area about 4 cm in diameter There were no pseudopodia

Lesions were produced experimentally by heating the arm in water at 45 C and were excised a biopsy specimens In the first case 1 sweat duct showed intercellular edema and

(8) Brit J Dermat 0 166 1/0 May 1 8

partial disruption of the lining cells in the superficial part of the duct at the point where it passed into the epidermis There was some fluid exudation into the dermis at this site Although the duct opening showed a keratotic ring no proof of pore closure could be demonstrated in serial sections In the second case the sweat duct was tortuous and the lining cells at the superficial end were separated by edema There was a vesicle in the epidermis in close apposition to the sweat duct There was no evidence of pore closure

The findings suggest that the lesion that has been called cholinergic urticaria is not primarily a dermal edema but is a spongiotic epidermal lesion having many features in common with the changes described in prickly heat Lesions resembling urticarial wheals could conceivably occur in cholinergic urticaria if exudation of sweat from a disordered sweat duct took place mainly from the subepidermal part of the duct The increased whealing under collodion noted by Grant and co workers in this condition would be expected if the disease were analogous to prickly heat which is accentuated by maceration and by adherent substances such as adhesive plaster and collodion Further the small pale papule surrounded by a large flare seen in these cases is not typical of histamine urticaria

Lanolin has been recommended for use in miliaria on the ground that softening the keratin plugs will allow free drainage of sweat ducts These 2 patients were not benefited by lanolin applications but after mild exfoliating doses of ultraviolet light twice weekly for 2 months they were free from urticarial lesions for 20 and 6 months respectively

► [The well known evanescent lesions of cholinergic urticaria could hardly be explained as a process taking place in the epidermis Spongiosis undoubtedly requires much more time to develop and to disappear than it takes for the wheals of cholinergic urticaria to come and go

There is no question that sweat does contain urticariogenic agents Sulzberger et al (J Invest Dermat 21 293 1953) found that when sweat ducts are obstructed while the secreting acini maintain their function autogenous sweat which is forced into the tissues can produce discomfort itching and clinical and subclinical wheals Further if an epidermal process as the one described was responsible for the whealing one would expect similar wheals to occur with miliaria—which is not the case —Eds]

Light Dermatoses F P Scott and S M C Molhuysen v d Walle[9] (Univ of Amsterdam) tested the sensitivity of patients with various light dermatoses to different wavelengths of the solar spectrum Included were 19 patients with dermatitis solaris 27 with prurigo aestivalis and 18 with chronic discoid lupus erythematosus The following skin reactions and methods to evoke them were used to estimate sensitivity (1) For sunburn erythema caused by wavelengths of 297 302 mμ a monochromator was used (2) For direct pigmentation caused by near ultraviolet rays of 320-460 mμ a Philips sun lamp was used for 10 minutes at 30 cm a sunburn reaction was prevented by inserting a 1 mm thick glass slide between the lamp and irradiated skin (3) For direct erythema caused by heat and infrared rays a Philips sun lamp (ultraviolet and infrared) was used for 10 minutes at 30 cm with a 1 mm glass slide inserted to prevent sunburn reaction

The studies showed a difference in sensitivity to erythema producing rays in the three types of light dermatoses investigated Patients with dermatitis solaris were more sensitive to the short sunburn rays than normal persons and also showed more secondary erythema reactions to long rays Patient with prurigo aestivalis showed a diminished reactivity to the sunburn spectrum no deviation of normal reaction to the long direct erythema producing rays could be demonstrated Patients with chronic discoid lupus erythematosus did not show a sunburn reaction deviating from normal and showed no hypersensitivity to ultraviolet rays as is generally accepted They did show however an increased sensitivity to the long direct erythema producing rays Rays longer than the sunburn producing ones may be responsible for certain dermatoses without the occurrence of sensitizing substances

► [It is possible that various parts of the light spectrum may cause dermatoses without the occurrence of sensitizing substances However it is not clear to us how the tests reported in this article prove this The findings of *diminished* sensitivity to the sunburn part of the spectrum in patients with prurigo aestivalis is contrary to the reports of other investigators (Epstein S J Invest Dermat. 5 187 1942) —Ed]

(9) Dermatologica 116 96 104 1958

Photoallergy and Photocross Sensitivity to Phenergan® occurred in a patient observed by Stephan Epstein and Richard J Rowe[1] (Marshfield Wis Clinic) The patient had a dermatitis due to Phenergan® sensitivity and photosensitivity superimposed on a dermatitis of unknown origin The photosensitivity was induced by oral administration of the drug at no time had the patient used Phenergan® externally A short period of elimination of Phenergan® during the early stage was followed by improvement and resumption of the drug by aggravation Patch tests and photo patch tests *demonstrated* that the patient apparently was contact sensitive to Phenergan® only but photoallergic to Phenergan® and chlorpromazine Both drugs are phenothiazine derivative

In photosensitivity a distinction must be made between phototoxic and photoallergic mechanisms Phototoxicity refers to those nonallergic phenomena which can be produced at will provided enough of the drug and proper rays are used Photoallergic reactions on the contrary are not normal obligatory reactions they occur only in a certain number of persons By no means all perhaps only a few cases of photosensitivity from phenothiazine derivatives are based on photoallergy

A peculiarity of photoallergy to phenothiazine derivatives is that many patients so affected exhibit a double sensitivity a plain contact sensitivity against Phenergan® or chlorpromazine itself and a photocontact sensitivity to a presumed oxidation or decomposition product of these drugs formed in the skin The photoallergic reaction apparently is an allergic response independent of the plain contact sensitivity

Photocross sensitivity between Phenergan® and chlorpromazine may exist though plain contact sensitivity (without light) can be demonstrated to only *one of the drugs* This was shown in this patient who was contact sensitive to Phenergan® only but photoallergic to both drugs

► [Photoallergy is assuming an increasing importance probably due to the mounting number of synthetic substances to which we are all exposed and the fact that some have photoallergic properties It will probably be necessary in the future to test new synthetic drugs contactants etc not only for their allergenic properties but also for possible photoallergic activity There was *photocontact* cross sensitivity but *no contact* cross sensitivity between Phenergan® and chlorpromazine in *Epstein and Rowe's*

[1] J I t Dern 29 319 326 November 1957

patient The most reasonable explanatic i for this difference in response is that exposure to light resulted in a transformation product from both substances which had contact allergenic properties This would be in cn sonance with the simplest and most reasonable hypothesis of the mecha nism of photoallergy light is essential only for release or production of the actual allergen and from there on the reaction proceeds as any other allergic reaction without the necessity for light—Eds]

Photoallergic Eczema Due to Blankophores (Optic Bright ening Agents) was studied by W Burckhardt (City Out patient Clinic for Skin Diseases Zurich) Many skin di ea es affect only the areas exposed to light and are aggravated by light In some diseases light appears to be the only causative factor There are exogenous endogenous and infectious fac tors which combined with light lead to diseases The blank



Fig 7—Photoallergic eczema after use of det rgent contain ng bla kophores. (Courte y of Burckhardt W Hautarzt 8 486-488 N mbe 1957)

(2) Hautarzt 8 486-498 No ember 195

ophores play an important role among the compounds that through external application lead to photoallergic reactions During the last few years optic brightening agents have been added to detergents white paper and to textiles to transform the invisible ultraviolet light into visible blue If the solution of such detergent is viewed under a Wood light vivid bluish fluorescence becomes apparent These blankophore substances are chemically related to the sulfonamides

The author observed 2 patients in whom after use of detergents containing brightening agents eczema developed in light exposed skin areas on the face hands neck and forearms (Fig 7) Restriction of the eczema to light exposed areas suggested the possibility that the sun rays played an etiologic role The author therefore exposed a skin area that had been pretreated intensively with the detergent solution in question to radiation from a Kromayer lamp filtering out however the erythema producing ultraviolet part of the radiation The radiation led to severe eczematous reactions The eczema recurred in each patient on re exposure to the same detergent One patient recovered completely but the other had recurrences of eczema due to light sensitivity

► [Thus far no cases have been reported in the United States of photoallergic eruptions due to blankophores in soaps and detergents These substances also are called optical bleaches brighteners whitening agents and fluorescent bleaches (Villaume F C J Am Oil Chem Soc 35 5 8 1958) Many different types of chemical compounds are in use and according to the best information available to us it is no longer *possible to buy* a laundry soap or detergent in the United States which does not contain one of these substances This of course does not mean that *any of the* substances used in this country necessarily are potential causes of photoallergic reactions in man Nevertheless here is another *example of possible* harm from the growing number of additives to foods drugs contactants and other materials to which we all are *exposed daily* usually unbeknown to even the best informed among us

Nonfluorescent dyes on cloth reflect part of the visible light which we then *perceive as color The* nonreflected part is converted into longer (infrared) wavelengths and therefore is radiated as heat The fluorescent dyes on cloth absorb practically no visible light Instead they absorb invisible ultraviolet light and *reflect it as visible blue light* thus causing the extra white appearance of the cloth —Eds]

Clinical Picture and Differential Diagnosis of Lupus Erythematosus Like Light Eruptions According to G Weber[3] (Mainz Germany) lupus erythematosus like light eruption must be differentiated from chronic lupus erythematosus Although sunlight causes the former it only influences the lat

(3) Hautarzt 9 400 406 September 1958

ter Light eruption affects only light exposed areas e pecial ly the face but chronic lupus erythematosus may under certain circumstances involve any area of the body

Sharply circumscribed moderately elevated round oval or polycyclic lentil to silver dollar sized carmine red patche which often appear in groups make up the picture of light eruption The smooth surface of the lesions is soon changed by scaling causing them to resemble lupus erythematosus In the latter strong adherence of the scales to the skin pro nounced hypersensitivity and atrophic zones usually start ing in the center of the lesions make differentiation from lupus erythematosus like light eruption possible Subjective symptoms such as burning and itching may be present in both diseases

Histologically light eruption is characterized by mild to moderate hyperkeratosis In one of the author s patients parakeratosis was also present Intraepidermal and intracu taneous edema and perivascular mainly lymphocytic infil trations dominate the picture The dilated blood filled vessels show no proliferation of the intima or media Elastic fibers are preserved in their structure and continuity The subepi dermal border zone has normal width bounds and staining properties

Chronic lupus erythematosus is characterized by hyper keratosis that affects mainly the follicles by atrophy of the epidermis and cutis liquefaction necrosis of the basal cells and lymphocytic infiltration around the skin appendages The collagen fibers are also involved The main differential characteristic is behavior of the P AS reactive subepidermal border zone which shows considerable widening especially during exacerbation

Therapy consists of light protective ointments nicotinic acid Atabrine® and chloroquine The last drug appeared to be effective in both chronic lupus erythematosus and lupus erythematosus like light eruption

Trial to Classify Light Eruptions According to Pathogen esis W Burckhardt[4] (City Clinic for Skin and Venereal Dis eases Zurich) investigated the toxic or allergic role of light in the cause of light eruptions Antibodies can be shown only in a few allergic diseases in general Similarly antibodies

(4) De matolog ca 116 ? 3 9 Ap May 1958

would be expected to be found only in ome instances of allergic light eruptions Individual hypersensitivity to rays of the sun or to rays of the sun plus an additional factor has to be proved by various test methods Light eruptions classified in the table may be due to light alone to combined light and

PATHOGENESIS OF LIGHT ERUPTIONS

I H A E	L H E OG- O S F C E CT VE	L H ND E DOG- S F T E F CT VE	LIGHT IN C T L F CT EF CT S
	Toxic Pathogenesis		
Phototrauma	Photosensitiza tion through plants dyes coal tar	Hydroa vacciniforme in congenital familial porphyria	Photobiotrop ism
Sunburn			Herpes solaris
Light cancer			Actinic exan thema in lym phogranuloma inguinale
Xeroderma pig mento um			
Cheilit s solaris			
	Allergic Pathogenesis		
Actin c urti caria	Actinic exan thema due to sulfanilamide phenothiazine	Polymorphonu clear actinic exanthema	
	Para amino- be zoic acid ester	Allergy to Kim mig substance or to porphy rins	
	Fara amino- salicyl c acid		
	Flankophores		

endo or exogenou noxious factors or to photobiotropism when light causes exacerbation of a latent infection

When determining hypersensitivity to light the various wavelength must be tested separately In absence of large spectrographs filters must be used that are permeable only to certain egments of the pectrum The erythema producing wavelength of 2800 3150 Å alone rarely cause derma

toses. Often there is hypersensitivity only to rays with wave lengths of 3,150-4,000 A. With the latter rays the normal skin can be irradiated for 30-60 minutes, causing only slight reddening and light immediate pigmentation. Nodular or vesicular reaction is pathologic.

► [A useful working classification of the light eruptions. Occasionally it may be difficult to ascertain whether the exogenous pathogenic factor (e.g., sulfanilamide, para-aminobenzoic acid, certain dyes, plants, etc.) plays a phototoxic or photoallergenic role.—Eds.]

Sensitivity to Fluorescent (Blue-Green) Light. In most cases of solar erythema previously reported in which light tests have been elicited, the action spectrum was below 3,900 A. John H. Lamb, Phyllis E. Jones, Gerbert Rebell and Herman D. Alston[5] (Oklahoma City) report 4 cases of erythema perstans type of sensitivity to visible fluorescent light in the range of 4,000-7,000 A.

Schoolteacher, white, 45, noted redness and burning of the face and neck after several hours driving in a new car which had antiglare bluish violet pigments incorporated in the windshield. This phenomenon recurred each time she rode in the car. The next month she noted burning and redness of the exposed areas of the skin when she walked home from school for lunch. When she returned to school the erythema quickly subsided. However, each day the redness and burning lasted a little longer. One month later she observed that after her 30 minute toilette in the bathroom she had the same symptoms. White fluorescent bulbs were used in the fixtures on each side of the bathroom mirror. She consulted an allergist who made the diagnosis of a blue light sensitivity. He prescribed chloroquine, 400 mg. once daily, and a light screening ointment (A-Fil). No appreciable improvement ensued.

When first examined by the authors, the exposed skin on the arms and below the knees showed a deep red erythema. The neck showed poikiloderma-like changes, and there was persistent erythema of both cheeks. Exposure of a 3×4 in. area of the back to two 5 watt fluorescent lights (white bulb) at 6 in. distance resulted in a faint patchy erythema in 9 minutes. At 15 minutes there was 4+ erythema and urticaria with severe itching. When a frosted glass 2 mm. thick was inserted between the light source and the skin, exposure for 15 minutes produced only faint erythema. However, there was a delayed reaction to 2+ intensity 10 minutes later. Eight minutes' exposure to a 100 watt incandescent light with a known light source of 4,000-7,000 A at 19 in. from the skin caused an urticarial response. Addition of frosted glass failed to decrease the reaction to this more powerful light source. Skol® (absorption spectrum 2,500-3,200 A) was placed over the skin exposed to both fluorescent and incandescent light. It caused no appreciable change in the erythematous reaction.

(5) A.M.A. Arch. Dermat. 7[illegible]:195, May, 1958.

Therapy consisted of removal of fluorescent light sources and weekly injections of testosterone After 4 months the patient s skin became tanned and all tests to blue light were negative

Because of the popularity of fluorescent lighting the dermatologist should be cognizant of its photosensitizing action in erythema solare subacute lupus erythematosus and polymorphic light eruptions that fail to clear with antimalarials These drugs seem to protect patients from the action spectrum approximately at the end of the sunburn spectrum 3 100 to about 3 600 A

► [In this particular instance and for the sake of clarity it would be better to refer to the action spectrum which elicits the light sensitive eruption rather than the source of the light or the color emitted as different substances produce fluorescence at different wavelengths of light. Of course Lamb and his collaborators are referring to sensitivity to light emitted by fluorescent light bulbs rather than fluorescent light.

The increasing interest in photodynamic and photoallergic sensitization gives promise that the very wide gaps in knowledge in this field will gradually be filled Classification of these eruptions based on the eliciting wave lengths of light and on their morphologic characteristics is only a first step However the principal task still remains to ascertain what substance or substances in the skin actually produce the abnormal sensitivity to light. These could be abnormal endogenous metabolites or exogenous substances (in a chemically altered or unaltered state) or they could be combination products of exogenous substances with autochthonous products.—Eds]

Urticaria Like Reaction after X ray Treatment G Weber[6] (Univ of Mainz) reports a case

Man 69 was given x ray treatment for several basal cell epitheliomas on the face and trunk Dose was 500 r and the factors were 4 cm focus skin distance no filter 50 kv and 2 ma Erythema and urticaria like lesions appeared in the treated areas 6 hours later In areas where treated lesions were close together a diffuse urticaria like swelling appeared apparently resulting from overlapping of roentgen rays Tests with various total dosages of roentgen rays given at 55 kv and with varying kilovoltage but constant quantity of x rays (500 r) indicated that the urticaria-causing effect of the roentgen rays was more dependent on total dosage than on the voltage induced wave length

Serum of a cantharides blister of the patient was transferred to a control patient in 1 24 hours later the area was treated with 500 r An inflamed urticaria like eruption developed after 4 hours on the treated site and disappeared within the next 24 hours A similar reaction resulted when serum from the patient was treated with 500 r x rays before being transferred to the control subject Similar tests with blister serum from normal controls gave negative results Use of a sulfhydryl containing compound (5cysteine) as protection from the effect of x rays did not prevent the urticarial response that resulted when the patient s serum was used in these experiment

(6) T J [illegible] Derm t 30 311 313 J [illegible] 1953

These findings demonstrate that the human skin can be sensitized not only to visible light but also to considerably shorter electromagnetic waves (roentgen rays) The presence of an antigen antibody reaction is proved by the passive transfer of the antibodies Roentgen rays do not have the characteristics of an antigen but probably liberate an antigen as evidenced by the results of irradiation of the patient s serum in vitro That the use of a sulfhydryl compound as protection from radiation could not stop the development of the urticaria like eruption is unexplained

► [The patient s urticaria like reaction to roentgen rays is most unusual Some of the results of the immunologic studies reported here are difficult to reconcile with previous findings in the field of hypersensitivity to other physical agents Passive transfer by the blister fluid technic is not generally considered an acceptable method Previous attempts by other investigators to produce the allergen in vitro by exposure of the patient s blood serum to light or cold have failed—Ed]

Influence of Varying Physical Factors on Patch Test Responses was studied by William A Anderson Harry Shatin and Orlando Canizares[7] (VA Hosp Bronx N Y) Patch tests were performed with 5 mm high wood squares and wood disks with smoothed edges and with similar wood squares and disks with edges rounded off completely Twenty seven 26 and 25 subjects were tested with 18 mm squares of sponge rubber 5 mm 10 mm and 15 mm high respectively An appreciable number of reactions resulted where the wood squares and disks with smoothed edges were used but no reactions were observed in a series of 20 tests with wood squares and disks with rounded edges With the 5 mm rubber squares 25 of the 27 subjects tested showed no reaction 30 minutes after removing the patch No subject showed evidence of reaction after 24 hours The 10 mm high rubber squares produced reactions similar to those produced by the wood square or disk both qualitatively and quantitatively with about 35% of subjects showing a reaction after 24 hours With the 15 mm high squares of rubber the reactions were more marked qualitatively and quantitatively over 50% of the subjects reacting at 24 hours

The nonspecific reactions observed with wood disks and squares and with thick squares of sponge rubber occurred primarily at the margins of the test site The marginal nature of the reaction to wood squares and disks with smoothed

(7) J Invest Derm 30 78? February 1958

edges in contrast to the absence of reaction to the wood disks and squares with rounded edges indicates that the reactions were due to the traumatic effect caused by what is basically a cutting edge resulting from pressure If an elastic substance such as sponge rubber is thick enough and sufficiently compressed it can also produce a nonspecific traumatic effect

In performing patch tests with hard substances the possibility of these nonspecific reactions should be considered Pressure can also potentiate a patch test with an allergen particularly at higher dilutions or in persons with a low degree of sensitivity

► [The incidence of false positive reactions obtained by the authors is an indication that any variations in established and time tested technics of patch testing cannot be made without carefully planned and thorough investigation —Eds]

Occurrence of Urticaria (Erythema) Due to Both Cold and Heat Urticaria and/or erythema from cold or heat is a well known phenomenon However cases of urticaria or erythema from both cold and heat are rare George Rajka Jr and Elizabeth Vincze[8] report 2 cases

CASE 1 —Man had urticaria during cold weather with a remission in spring but during hot weather the urticaria recurred Local urticaria resulted from contact with cold running water (28 C) and hot running water (42-44 C) Urticaria also appeared after drinking hot tea after exposure to heat psychic stimuli and exercise

CASE 2 —Man 24 had patches of erythema on the skin after contact with cold air after a cold bath and after hurrying and getting hot The erythema persisted 1 3 hours Exposure to hot or cold water ice or chlorethyl spray caused erythema but not urticaria Erythema also occurred after drinking hot tea exercise emotional disturbances and subcutaneous injection of 10 mg pilocarpine

Some of these findings suggested an allergic mechanism whereas others seemed to indicate a nonallergic cause The exact pathogenesis has not been determined In favor of an allergic mechanism the authors list (1) occurrence of sudden attacks (2) positive dermal and exposure tests (3) presence of itching and (4) a refractory phase after positive tests Evidence for a nonallergic mechanism includes (1) presence of symptoms after both heat and cold (2) negative passive transfer (3) diminished pathologic response during prolonged drug induced sleep (4) absence of personal and family history of atopy and (5) presence of focal infection

► [The first case resembles cases described by Hopkins Kesten and Hazel

8) Act Derm 12 30 38 1958

(Arch Dermat u Syph 38 679 1938) As pointed out by Rajka and Vincze the question as to whether both the heat and cold urticaria in these cases or only one of these or neither is based on an allergic mechanism cannot be definitely answered at present —Eds]

4 DRUG REACTIONS

Severe Reactions to Antibiotics Nationwide Survey of hospitals comprising about one third of all general hospital beds in the United States is reported by Henry Welch C N Lewis, H I Weinstein and B B Boeckman[9] (Food and Drug Admin) All severe reactions occurring in these hospitals from late 1953 to early 1957 were investigated and classified

Of available antibiotics penicillin was found to produce the greatest number and the most severe reactions Of 1 070 reactions considered to be life threatening 901 were due to penicillin Anaphylactoid shock the most frequent serious reaction to penicillin resulted in a fatality rate of about 9% Most reactions to the drug occurred when it was given intramuscularly No deaths resulted from its oral administration Of 1 925 reactions classified as not severe or life threatening 1 616 were due to penicillin

In order of frequency the life threatening reactions to antibiotics were shock superinfections severe skin reactions blood dyscrasias and angioneurotic edema with respiratory tract involvement The most frequent minor reaction was angioneurotic edema and urticaria The broad spectrum antibiotics caused relatively few adverse reactions Tetracyclines accounted for most cases of severe superinfections Of these enterocolitis was the most common and most severe It occurred particularly often in patients undergoing abdominal surgery and mortality was high The commonest severe dermal reaction was exfoliative dermatitis of which 10% of cases were fatal Erythema multiforme and anaphylactoid purpura accounted for the other severe dermal reactions 1 case terminated fatally In the blood dyscrasia group aplastic anemia was the most common accounting for 23 of 27 deaths Blood dyscrasias were most often associated with use of chloram

(9) Antibiotic Med & Clin Therap 4 800 813 December 1957

phenicol Angioneurotic edema with involvement of the respiratory tract was commonly caused by intramuscular injections of penicillin 38 cases were reported with a fatality rate of 13%

The survey re emphasizes the need for caution in administering antibiotics A study of case histories did not reveal indiscriminate use of penicillin by physicians but rather an expected increased incidence of reactions through wide use of a highly antigenic substance

► [An important and informative article which should be read in the original It is evident that although the over all incidence of systemic reactions from penicillin is small considering the number of injections given and tablets taken per year the reactions can be so severe even including death that this antibiotic should be considered a potentially "dangerous drug To think of penicillin in this way will not preclude its use but will make the physician review all facts before deciding to administer it *by injection*

Just as with other categories of drugs antibiotics must be selected not only for their spectrum of antibiotic effect but also with regard to the undesirable reactions which may occur The physician should be prepared to cope with severe reactions resulting from the antibiotic and the patient as well should be briefed as to what course to follow in the event of undesirable reactions —Eds]

Dermatitis Medicamentosa Due to Diuril® (Chlorothiazide) Report of Three Cases is presented by James R Rogin[1] (Detroit)

CASE 1—Woman 37 had a brightly erythematous and papular eruption with a few scattered papulovesicles on the upper and lower extremities The eruption appeared 8 days after she took chlorothiazide 250 mg twice daily for 2 days for premenstrual edema It was accompanied by much edema of the ankles lower legs and hands There was no history of ingestion of other drugs The eruption persisted 2 weeks during which time the patient was treated with antihistamines colloid baths and a lotion

CASE 2—Woman 62 was given chlorothiazide 250 mg twice daily for 10 days at which time a generalized erythematopapular eruption appeared on the trunk and extremities There were also many purpuric lesions The eruption disappeared completely 2 weeks after chlorothiazide was discontinued although other medication for cardiac congestion was continued during this time

CASE 3—Woman 4? had taken chlorothiazide irregularly *for 6* months for premenstrual edema and tension During the 6th month she took 500 mg chlorothiazide once daily for 8 days On the 8th day an erythematopapular eruption appeared and spread over the upper and lower *extremities* and neck The eruption was accompanied by edema of the feet lower legs and hands Because of the *intense pruritu*

[1] J A M A Arch Derm t 8 04 505 Octobe 1958

he was treated with triamcinolone The eruption disappeared within 1 week but severe pruritus was still present

► [We have heard also of several cases of photo sensitization dermatitis due to Diuril® —Eds]

Dermatitis Caused by Penicillin in Milk Since the introduction of machine milking the incidence of mastitis in cows has increased and the common practice among herdsmen is to inject 100 000 units of procaine penicillin into the teat of the infected quarter As a result of this treatment milk may contain penicillin If patients previously sensitized to penicillin drink milk containing penicillin dermatitis may develop and persist indefinitely if its true nature is not recognized H R Vickers L Bagratuni and Suzanne Alexander (Radcliffe Infirm Oxford England) report 2 cases of dermatitis apparently due to penicillin in milk

Case 1 —Woman 55 had had recurrent attacks of dermatitis for 6 years History revealed several attacks of contact dermatitis due to various allergens including penicillin She had lived on farms for many years One year before the present severe attack of dermatitis she had her own cow which had not been treated with penicillin During this time she had no recurrences of dermatitis When her cow stopped lactating she drank fresh bulked milk and had a relapse Analysis of this milk showed a penicillin content of 4 units/ml Desensitization to penicillin was carried out starting with 1 unit intramuscularly This treatment was continued until she was able to tolerate 1 000 000 units The dermatitis cleared and she was able to return to drinking cow s milk without relapse

Case 2 —Man 44 had an acute generalized vesicular dermatitis He had been treating his cows with penicillin for mastitis off and on for 2 years He had started to treat 1 cow 10 days previously Milk from this cow had been added to the rest of the farm milk which he had been drinking Patch tests were positive for penicillin The eruption subsided rapidly under treatment with prednisolone

The American Food and Drug Administration has ruled that milk from any cow treated with penicillin should be discarded for 72 hours This order however is not universally observed and sometimes penicillin may even have been added to milk as a preservative In Britain there is an indefinite ruling that milk from infected cattle shall not be distributed Because mastitis can often be diagnosed early and penicillin usually produces a rapid cure most of the milk from mildly infected cattle is distributed in the normal way Since the number of persons sensitive to penicillin is increasing with wider use of the drug the authors feel that

(?) Lancet 1 351 35 Feb 15 1958

the American ruling prohibiting distribution of milk for 72 hours after treatment of mastitis should be adopted in Britain

► [Another of the many hidden sources of allergens which threaten man living in our modern civilization We also observed a patient in whom all the evidence including tests of avoidance and re exposure pointed toward a fixed urticarial reaction due to penicillin in milk —Eds]

Sensitivity to Repository Penicillins R R Willcox and G R Fryers[3] (London) present a retrospective study of the side effects observed after administration of 7 300 injection of four repository penicillins penicillin in oil and beeswax procaine penicillin with aluminum mono stearate benzathine penicillin and benethamine penicillin The injections were given 895 patients during 11 years

The over all incidence of probable reactions was 2 9% of patients and 0 4% of injections If all possible reactions are included the figures are 4 8 and 0 6% respectively The incidence of reactions was low after single injections but increased with the number of injections up to 9 after which there was an apparent fall No reactions were noted with a dosage of less than 1 mega unit the bulk being found in the 1 19 9 mega unit total dosage range with a marked fall thereafter by which time most of the sensitivity likely to occur had probably declared itself The incidence of reactions in patients known to have had penicillin previously was 3 6% compared with 2 8% in patients not known to have had previous treatment Patients with leg ulceration were particularly prone to sensitivity probably because of previous topical use of penicillin

There was no significant difference in the incidence of reactions to the various types of long acting penicillin and no evidence of unusually prolonged or delayed reactions after the use of repository penicillin One fatality occurred This was due to bronchopneumonia complicating dermatitis after penicillin in oil and beeswax No unequivocal anaphylactoid reactions were observed

Cutaneous Eruptions after Use of Salk Poliomyelitis Vaccine Despite mass vaccination of children and adults against poliomyelitis the incidence of cutaneous eruption is extremely low George M Stroud Harold L Brodell William P Lascheid and Lew W Potts[4] (Univ Hospitals Cleve

(3) Brit J Ven Dis 33 09 16 December 19 7
(4) J A M A 166 251 2 1 J 18 1958

land) report 12 cases Most dermatoses were fairly severe but none was serious and all subsided Seven of the 12 patients had received penicillin previously One was sensitive and another questionably allergic to it Nine had dermatoses considered to have important allergic components

Urticaria occurred in 4 cases In Case 1, the patient had had mild urticaria before he received Salk vaccine but a sharp attack occurred 6 days after the first injection After a vaccine with a substantially lower penicillin content was used a month later no urticaria developed In Case 2 a girl 3 had fever malaise and urticaria after every Salk vaccine injection and also after an injection of diphtheria, pertussis and tetanus vaccine and toxoids which contained no penicillin In Cases 3 and 4 the patients had a delayed type of allergic eruption with urticaria joint pains and a constitutional reaction

An eczematous eruption appeared to be precipitated reproduced or exacerbated by inoculation against poliomyelitis in Cases 5 through 9 The incubation period in this group was shortest averaging 4 days Only 1 of the 5 patients was known to have received penicillin before, and he had no history of previous sensitization This was the only patient in the group to be revaccinated and the eruption reappeared after the second injection of Salk vaccine

In Case 10 man, 36 had a psoriasiform eruption after taking penicillin for a severe upper respiratory infection After an injection of Salk vaccine which contained the standard amount of penicillin he experienced a similar attack In Case 11, the patient a sister of the patient in Case 10 had an acute eruption consisting of red scaly oval patches on the extremities after each of two vaccinations against poliomyelitis In Case 12 a penicillin sensitive patient exhibited an extension of her psoriasiform dermatitis soon after receiving an injection of Salk vaccine

Contrasted with some cases reported in this study most penicillin reactors and persons with eczema and psoriasis were vaccinated against poliomyelitis without untoward reactions Salk vaccine is suspect in the reported eruptions but if it is responsible the causative ingredient or ingredients cannot be determined from the data submitted

► [Although the agent causing the reactions following administration of

the Salk vaccire is not known for all the patients presented the fact that it was the penicillin in the vaccine which was responsible in some instances should alert physicians to be prepared for counteracting untoward reactions not only to the active ingredient but also to adjuvant materials or contaminants (silk!) contained in a drug (see Brown *et al* J.A.M.A 165 2178 1957) —Ed]

Penicillin Combined with Gamma Globulin as Diagnostic Agent in Urticaria of Serum Sickness Type Due to Penicillin George Rajka Jr and Elizabeth Vincze (Stockholm) found that 0 05 ml of a mixture containing 10 000 I U of crystalline penicillin and 1 ml of 10% gamma globulin was more effective than crystalline penicillin alone for diagnosing urticaria of the serum sickness type due to penicillin In 34 of 40 cases intracutaneous reactions were obtained with the combined testing agent compared with 16 with crystalline penicillin alone The combined agent did not produce pseudopositive reactions in doubtful or negative cases of penicillin allergy or in controls

Reaction was immediate in about 75% of patients who had reactions to the gamma globulin penicillin combination When a preparation that had been stored for more than 3 weeks and had become moderately opalescent was used reaction was seldom immediate but delayed or doubtful reactions increased This confirms that the purer an allergen is the more likely reactions are to be immediate Frequently both immediate and delayed reactions occurred in the same person The authors have no explanation for this

In 9 of 18 passive transfer tests the gamma globulin penicillin combination yielded a positive reaction and in 4 a doubtful reaction compared to only 2 positive reactions and 1 doubtful reaction obtained with penicillin alone Of 6 patients who showed both immediate and delayed intracutaneous reactions 5 showed passive transfer reactions the 6th had a doubtful reaction Of 5 patients who had only immediate intracutaneous reactions 1 had a passive transfer reaction and 2 had doubtful reactions Of 6 patients who showed only delayed intracutaneous reactions 2 had passive transfer reactions and 1 a doubtful reaction One patient who had no intracutaneous reaction had a transfer reaction Hence there was no correlation between Prausnitz Kustner reactions and immediate or delayed intracutaneous reactions

► [The occurrence of positive passive transfer tests with the serums of

subjects who had only delayed positive reactions and 1 subject who had neither an immediate nor a delayed intracutaneous reaction is most unusual!—Eds.]

Visceral Lupus Erythematosus as Side Effect of Treatment with Hydantoin Derivates is discussed by H. Rupp and R. Vossen.[6] Hydantoin derivates have been used for years in treating epilepsy because of their reliable anticonvulsive effect. The most commonly used compounds are 5,5 diphenyl hydantoin and 3 methyl 5,5 phenylethylhydantoin (Mesantoin) administered singly or combined with other antiepileptic drugs.

The following side effects to hydantoin therapy have been described previously: skin changes (exanthema), gum changes (hyperplasia), generalized swelling of the lymph nodes, gastrointestinal disturbances, central nervous system involvement (somnolence, dizziness, ataxia, tremor), vascular changes as periarteritis nodosa and liver damage (central lobular necrosis). Occasionally the blood of hydantoin treated epileptics has shown a positive L.E. phenomenon.

The authors describe 7 patients, 5 females and 2 males, aged 11-63, in whom after varying periods of treatment with hydantoin derivates, visceral lupus erythematosus developed with positive L.E. phenomenon in the blood. In the following 3 the disease was fully developed clinically, whereas the other patients had only subclinical manifestations.

CASE 1.—Woman epileptic, 22, received 500 gm. Mesantoin in 3 years. During the last year her general condition deteriorated and she lost 10 kg. body weight. Joint pains and swelling of the foot joint developed. Finally, septic temperatures set in; the finger joints swelled and exanthema appeared on the head, neck, trunk, upper arm and hand. There was pleural effusion on the right, leukopenia advancing almost to agranulocytosis, a very high sedimentation rate, an increase in alpha and gamma globulin, and positive L.E. cells in the blood. After Mesantoin was discontinued and Ultracorten® administered for 1 month there was striking improvement. After 3 months recovery was complete. Only the L.E. phenomenon remained positive after 4 months.

CASE 2.—Woman epileptic, 63, received in 6 years about 240 Gm. Mesantoin and 500 Gm. diphenylhydantoin. Five months after resuming Mesantoin therapy she became ill with attacks of fever, exudative pleurisy, joint swelling and pain and skin changes. The sedimentation rate was high, the alpha and gamma globulins were increased and the blood showed positive L.E. phenomenon.

CASE 3.—Man, 55, with presenile depression, received in preparation

(6) Schweiz. med. Wchschr. 87:1555-1558, Dec. 1, 1957.

tion for electric shock therapy 4 4 Gm Mesantoin in 9 days On the last day he had a high temperature morbilliform exanthema lymph node swelling and a greatly increased sedimentation rate One week later bilateral pleural exudate pulmonary infiltration and transitory leukopenia developed The alpha and gamma globulins were increased The blood showed a positive L E phenomenon After the discontinuance of Mesantoin and under penicillin and sulfonamide therapy all symptoms and signs subsided fa t

Most authors have assumed that pathogenically visceral lupus erythematosus consists of an antigen antibody reaction with the formation of autoantibodies which in vivo change the collagen connective tissue and in vitro produce the L E phenomenon In this reactive system drugs may act as haptens

► [We do not believe it is desirable to label patients as having visceral lupus erythematosus in those cases in which certain medicaments (e g Mesantoin) produce the signs and symptoms of subacute and acute lupus erythematosus including a positive L E cell phenomenon. It would be preferable to refer to such syndromes as lupu erythematosus like drug reactions due to Mesantoin.—Eds]

Eczematous Complications in Treatment of Tuberculosis Eruptions Resulting from Combined Aminosalicylic Acid Dihydrostreptomycin and Isoniazid Therapy were observed in 37 patients by John T Crissey Earl D Osborne and James W Jordon[7] (Buffalo) The lesions resembled nummular eczema seborrheic dermatitis or a combination of both The initial lesion in the form resembling nummular dermatitis (12 cases) were closely aggregated pruritic erythematous papules or papulovesicles which coalesced rapidly to form coin shaped eczematous plaques The sites most commonly involved were the lower parts of the leg especially about the malleoli the extensor aspects of the arms the anterior axillary folds the antecubital fossae the dorsa of the hands and feet the chest and the back The lesions were often localized in areas previously occupied by other dermatoses such as stasis dermatitis dyshidrosis dermatophytosis or dermatitis venenata though these conditions had been absent for many years Lesions that had been present for some time gradually became thickened and assumed the form of lichen simplex chronicus

The earliest change in the form resembling seborrheic dermatitis (6 cases) was the appearance of fine scaliness on the scalp e pecially at the hairline Later erythema appeared

(7) J.A.M.A 165 1526-1528 N 3 1957

and the eruption spread to the external auditory meatus retroauricular areas eyebrows nasolabial folds and occasionally the presternal area The lesions then became moist so that the picture closely resembled the exudative phase of seborrheic dermatitis except for response to treatment Itching was often intense and complicating pyoderma was common The commonest eruption was mixed resembling both nummular and seborrheic dermatitis (19 cases) In 2 such cases the lesions progressed to a generalized exfoliative dermatitis

Since the eczematous eruptions in patients treated with chemotherapeutic agents resembled so closely the common skin diseases nummular dermatitis and seborrheic dermatitis a definite relation to the antituberculous medications could be established only by prolonged observations By observing the drugs being given when the eruptions began and the response of the eruptions to selective withdrawal of the drugs the authors concluded that aminosalicylic acid was the chief cause that dihydrostreptomycin was an occasional cause and sometimes a prolonging factor and that isoniazid was not involved From the frequent finding of dihydrostreptomycin resistant micrococci in the skin lesions the authors postulated that a disturbance in the normal bacteriologic flora of the skin might underlie the eruptions

Management included an initial attempt at control by topical means without stopping administration of any of the tuberculosis drugs If symptoms became unbearable or if alarming extension of the eruption occurred aminosalicylic acid was withdrawn On this regimen many reactions subsided In severe cases steroids were used combined with the chemotherapeutic agents

► [Without the detailed observations of Crissey Osborne and Jordon implicating para aminosalicylic acid as the principal cause of the eruptions one would have thought that the dihydrostreptomycin was their cause Topically applied neomycin frequently causes seborrheic dermatitis like or psoriasiform eruptions and as was shown by Sidi et al there is an immunochemical relation between streptomycin and neomycin Previous reports of eruptions due to para aminosalicylic acid dealt with scarlatiniform and urticarial eruptions —Ed]

Cutaneous Reactions Due to Sulfamethoxypyridazine Donald G Lindsay (Ventura Calif) Isaac Pilmn (Virginia Minn) Arthur J Bischoff and S William Becker Sr [8] (Long

(8) A M A Arch Dermat 8 99 303 September 1958

Beach Calif) report the occurrence of an erythematous maculopapular dermatitis in 13 of 85 patients (15 3%) taking sulfamethoxypyridazine In 1 patient the dermatitis progressed to a severe generalized bullous and ecchymotic eruption In the other patients the eruption cleared promptly when the drug was discontinued Of the 13 patients with sulfonamide dermatitis 5 had taken sulfonamides previously Of the 72 who showed no reaction to sulfamethoxypyridazine 29 had taken sulfonamides previously Of the total 85 patients taking sulfamethoxypyridazine 2 (6 6%) of 30 taking 0 5 Gm daily doses showed an untoward reaction while 11 (20%) of 55 patients taking 1 Gm or more daily had dermatitis In general dermatitis occurred within the first 5 days in patients who had taken sulfonamides previously and after about 2 weeks in patients with no previous experience with these drugs

Daily serum sulfamethoxypyridazine determinations did not show a gradual increase with time at a constant dosage but averaged around 10 mg /100 ml in patients taking 1 Gm daily doses and 5 mg /100 ml in those receiving 0 5 Gm daily No correlation between reactions and serum levels of the drug was possible because too few determinations were made

► [The principal advantage of this sulfonamide (Kynex®) is that adequate blood levels can be maintained with 1 or 2 doses daily It appears doubtful that this convenience of administration is worth risking when the incidence of drug eruptions from its use is greater than 10% —Eds]

Melanosis Due to Camoquin® was observed by E Young[9] (Univ of Utrecht) in 3 cases within a short period Yellow scleras were also present and 1 patient exhibited partial pigmentation of anal and vulvar mucosa Skin biopsies showed an abnormally high melanin content mainly in the epidermis but also in the cutis The pigmentation may have been due partly to the Camoquin® itself

Man 43 had taken 300-400 mg Camoquin® daily for almost 4 months for chronic lupus erythematosus When examined he exhibited a brownish yellow color of the face neck (Fig 8) and dorsal surfaces of both hands and forearms Covered portions of the body were less strongly pigmented The scleras were yellow the mucous membranes showed no pigmentation The patient said that pigmentation had increased within a few weeks There were no subjective symp

(9) Nederl tijdsch geneesk 10 1088 109 J 1958



Fig 8 White plaque on right under jaw caused by lupus erythematosus and pigmentation of face and neck (Courtesy of Young F Nederl tijdschr geneesk 10 1088 109 June 7 1958)

toms Camoquin* therapy was stopped immediately Further studies showed no evidence of icterus liver function tests and proteins were normal Serologic tests were negative The scleral color was attributed to Camoquin* The skin color cleared after withdrawal of the drug

Hypervitaminosis A—Toxic Reaction D W Creek K J McNiece and L M Nelson[1] (Santa Barbara Calif) report toxic manifestations resulting from prolonged and excessive ingestion of vitamin A in 3 patients

Case 1 —Girl 16 was given 50 000 units of vitamin A 3 times daily for acne vulgaris On her own initiative without medical supervision she continued to take 150 000 units of vitamin A daily for over 2 years Because she began to lose her hair the intake of vitamin A was stopped immediately Two months later her hair had stopped falling out but 1 year later although she was much improved it had not returned to its original thickness The patient also experienced anorexia loss of weight and epistaxis which persisted until the vitamin A intake was discontinued

Case 2 —Man 47 took 200 000 units of vitamin A daily for generalized dry scaly dermatitis After 27 months on this dosage several large ecchymotic areas appeared on his extremities Bleeding time and clot retraction time were prolonged and the blood platelet count was 100 000 Three weeks after vitamin A was discontinued the plate

(1) Am J Gastroenter [illegible] 169 17 February 1958

let count was 147 000 the bleeding time was 1 minute and clot retraction time was normal There was no further tendency toward hemorrhage

CASE 3 —Man 67 had taken 200 000 units of vitamin A daily for 6 years He stated that his gums had bled intermittently for 3-4 years with profuse bleeding during dental extractions Blood counts bleeding and clotting time prothrombin time clot retraction and other laboratory tests were normal Four months after vitamin A was discontinued the remaining teeth were extracted without unusual bleeding He had no further hemorrhagic tendencies and remained asymptomatic

► [It is noteworthy that these 3 patients took much greater doses of vitamin A than those normally prescribed by responsible physicians It is probably safe to surmise that in this era of indiscriminate intake of vitamins many persons have undetected manifestations of hypervitaminosis A It should be remembered that the oil soluble vitamins A and D can produce toxic manifestations if taken in large enough doses for sufficiently long periods When prescribing vitamin A it would be wise to limit the prescription and to advise the patient regarding the proper use of this vitamin —Eds]

Severe Acidoketosis in Two Cases of Psoriatic Erythroderma Treated by Cutaneous Application of Salicylic Acid in Penetrating Fat Base is reported by E Sidi A Reinberg M Hincky and J Bourgeois Spinasse[2] (Paris)

CASE 1 —Young woman 33 whose general condition was poor had resistant psoriasis She was treated at home with salicylic acid in transesterified hydrogenated triglycerides (TTH) the only treatment the skin would tolerate This local treatment was continued after hospitalization besides oral medication with delta-cortisone and dihydrotachysterol General treatment was interrupted on the 20th day because of asthenia but local treatment with salicylated TTH was continued Four days later acidosis and coma supervened suddenly accompanied by Kussmaul's dyspnea ketonemia and ketonuria decrease in alkaline reserve moderate elevation of urea and glucose and potassium in the blood The patient died despite administration of glucose and bicarbonate solutions

CASE 2 —Man 50 with generalized psoriasis was treated on half the cutaneous lesions by salicylated lard and on the other half by salicylated TTH Four days after beginning these applications a precomatose ketosis developed with ketonuria decrease in alkaline reserve moderate increase of blood sugar and urea and significant salicyluria. Improvement eventuating in cure of the intoxication began after cessation of local treatment Salicylated petrolatum administered later caused no complications

The mixture of animal and vegetable triglycerides (TTH) is widely used by dermatologists because it is easy to use in preparation and application of ointments it is penetrating and produces no irritation or sensitization It was used by the

(2) Presse med 66 735 37 Ap 26 1958

authors in over 160 patients and in several hundred cases by others with no ill effects until these 2 cases were observed

Although the penetrating effect of TTH has distinct therapeutic advantages it also calls for caution when used to introduce substances that may be toxic in large doses An experimental comparison on 3 subjects of a petrolatum and a TTH pomade containing 1 5 Gm salicylic acid showed that blood salicylate 3 hours after application was 77 5 ± 5 mg/L with TTH and 30 5 ± 5 mg with petrolatum a difference of 60% Risk of drug accumulation is increased in sensitive skins of children or in those with extensive skin lesions as in psoriasis When such skin treatments are contemplated with use of an active or potentially toxic ingredient it is necessary to consider the extent of the area to be treated concentration of the active substance in the ointment and the age general condition and individual reaction of the patient

► [The fact that the active ingredients incorporated in lotions creams ointment or other vehicle may be absorbed through the skin and thus prove harmful systemically must always be kept in mind This pertains in particular to phenol and phenolic compound such as resorcin and tars ammoniated mercury chrysarobin salicylic acid and even boric acid. Dermatologic therapy should take into consideration the skin site where the pharmacologic action of the topical medicament is desired Very often superficial action is preferable to deep penetration —Ed]

Parathion Residues as Cause of Poisoning in Crop Workers is discussed by Griffith E Quinby (Wenatchee Wash) and Allen B Lemmon[3] (Sacramento Calif) The residue left after application of parathion as a pesticidal spray in field and orchards declines rapidly on most crops for the first few days and more gradually during ensuing weeks Mild poisonings have been caused in workers thinning picking cultivating or irrigating crops of apples pears grapes oranges and hops treated with 1 lb/acre or more of parathion Several known instances of poisoning involved exposure to foliage or fruit sprayed not more than 2 days before However contact with trees and vines has caused poisoning as much as 12 17 and 33 days after application of parathion In the episode occurring 33 days after spraying 16 workers in a vineyard were involved and the cause of illness was confirmed by low cholinesterase values and relief of symptoms by atropine The causal relation was further supported by the finding of a residue of 8 ppm parathion on the leave

(3) J A M A 166 740 46 Feb 15 1958

Although the vapor pressure of technical parathion doubles with a rise of temperature from 68 to 79 F the vapor pressure even at 103 F is only 1 µ Hg which is capable of producing at most a concentration of only 15 µg /L air It would seem most unlikely that workmen would be subjected to such saturated air for prolonged periods if at all However all thinners and harvesters have extensive contact between the fruit and their hands and less extensive contact between their arms and other parts of their body and the foliage Experiments have shown that the skin is the principal route of absorption even during actual spraying or aerosol operations Therefore it seems almost certain that dermal contact *is more important than inhalation in the poisonings* resulting from residues No one has estimated the importance of oral exposure resulting from eating drinking or smoking without washing the hands or from eating fruit while harvesting Dermal absorption is increased by removing shirts and other protective clothing and by wearing contaminated clothing for several days at a time

All outbreaks so far recorded have occurred from residues deposited on foliage at least chest high This may imply that workers are poisoned in this way only when dusted or bathed in the dilute residues practically from head to foot After 7 years of parathion use the lack of poisonings from residues on lower row crops appears significant

The chief symptoms of parathion poisoning are headache nausea vomiting diarrhea miosis weakness and mild shock Poisoning due to residues on foliage has been relatively milder with more gradual onset than that produced by exposure during spraying or dusting The relative mildness of the illness due to residues has probably caused many physicians to attribute such illness to causes other than the insecticides to which the crop workers were exposed Because of the paucity of published reports of poisoning by residues physicians have heretofore tended to insist on a history of direct exposure to sprays concentrates or dusts before considering a diagnosis of parathion poisoning Regulations intended to minimize the hazards of using parathion need to be reviewed with respect to the poisonings that have occurred from the persistence of toxic residues

► [Parathion is 0 0-diethyl-0 p nitrophenyl thiophosphate This cholines

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► [The fact that the active ingredients incorporated in lotions, creams, ointments or other vehicles may be absorbed through the skin and thus prove harmful systemically must always be kept in mind. This pertains in particular to phenol and phenolic compounds, such as resorcin and tars, ammoniated mercury, chrysarobin, salicylic acid and even boric acid. Dermatologic therapy should take into consideration the skin site where the pharmacologic action of the topical medicament is desired. Very often superficial action is preferable to deep penetration.—Eds.]

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(3) J.A.M.A. 166:740-46, Feb. 15, 1958.

there is hyperkeratosis This suggests that arsenic is bound in the keratin moiety

On the basis of his findings Scott proposes that in a person with a history of arsenical therapy and a persistently high skin content of arsenic administration of BAL should be considered to aid elimination of residual arsenic and thereby reduce the chances of development of malignant skin changes

► [The high levels of arsenic in the skin and especially in the epitheliomas and keratoses of these patients seem to settle the old argument whether increased quantities of this element are present in arsenical keratoses and epitheliomas Without examination of more patients who only recently have received arsenic it is not possible to decide whether there are significant personal variations in the ability to eliminate arsenic —Eds]

Arsenical Keratoses Associated with Carcinomas of Internal Organs Cases of visceral cancer after ingestion of or exposure to arsenic have been rare and definite evidence of arsenic being the direct cause of carcinoma in internal organs has never been presented M Rosset (St Joseph s Hosp Toronto) presents 2 cases of arsenical keratoses associated with visceral cancer One man 51 with cirrhosis and primary carcinoma of the liver had taken Fowler s solution for psoriasis off and on for about 20 years Another man 38 with a primary carcinoma of the head of the pancreas denied ingestion of arsenic but stated that in adolescence he worked on a farm where he used lead arsenate to spray potatoes The keratotic lesions on his palms appeared first while he was in his teens

In both these as in all cases reported previously the possibility of coincidence of arsenical poisoning and internal carcinoma cannot be ruled out However the carcinogenic properties of arsenic have long been recognized though experiments with it have produced only a few skin and other cancers in animals In some cases reported in the literature minute doses of arsenic have produced evidence of intoxication in others signs of intoxication have not appeared until many years after the medication had been discontinued and the patients were probably out of sight of their attending physician

Rosset feels that the benefits derived from arsenic in nonfatal diseases are not worth the risk of remote serious and

Canad M A J 7 416-419 31 1 1959

terase inhibitor apparently does not cause any visible cutaneous damage even though it exerts its poisoning effects via absorption through the skin —Eds]

Retention of Arsenic in Late Cutaneous Complications of Its Administration Until recently the smallness of pieces of skin available for analysis has limited the accuracy of methods for the chemical estimation of arsenic in that tissue By inducing radioactivity of the arsenic by irradiation in an atomic pile for 24 hours this problem can be circumvented provided standard weights of arsenic are irradiated at the same time Since all the other elements found in skin have a comparatively low specific activity and long half life the skin radioactivity detected by this method is attributable solely to its arsenic content The applicability of this method is limited to tissues which do not contain elements closely resembling arsenic in their radioactive isotopes

Using this method of measuring arsenic content A Scott[4] (St Bartholomew s Hosp London) found 0 4 1 μg arsenic/Gm wet weight tissue in samples of normal skin from patients with no history of arsenic intake In 7 of 9 epitheliomas removed from arsenic treated patients the arsenic content was over 1 8 μg /Gm The other 2 lesions gave values of 1 μg /Gm Two of 3 keratoses removed from arsenic treated patients had values over 2 μg /Gm Three of 4 biopsy specimens with the highest arsenic content were hyperkeratotic In 2 of 3 specimens of apparently normal skin of patients with a history of arsenic intake the arsenic content was greater than normal—1 8 and 2 μg /Gm Epitheliomas removed from 2 patients who had been exposed to external contact with arsenic for at least 20 years showed a high arsenic content (5 7 and 7 2 μg /Gm) despite a lapse of 10 and 25 years respectively since last exposure A specimen of normal skin removed from 1 of these patients contained 1 9 μg arsenic/Gm

The quantity of arsenic retained in the skin apparently bears no precise relation to the duration of intake of this drug nor to the time lapse since cessation of therapy This suggests a personal variation in ability to eliminate arsenic In patients who have taken arsenic the content of the element is greater in sites in which epitheliomas have developed than in the rest of the skin Levels are particularly high where

(4) Brit J Dermat 0 195 00 June 1959

the authors experience blood boric acid levels in fatal poisonings are of the magnitude of 50 100 mg /100 ml or more

► [There is no particular merit in the topical use of boric acid solution and boric acid ointment as compared with saline solution and plain white petrolatum or white petrolatum medicated with agents which lack systemic toxicity (e g Sterosan® Vioform®) Why then take a chance on accidental or the undoubtedly very rare therapeutic poisoning from boric acid? —Eds]

Nephelometric Studies in Drug Allergies were conducted by G Ziegler (Univ of Basel) Various tests have been developed to demonstrate allergens in vivo or in vitro In sensitized subjects the number of thrombocytes in the peripheral blood decreases more than 15% after exposure to relatively small amounts of allergen This test has been found positive with inhalation food and drug allergens This method can be applied also in vitro by adding various allergen dilutions to the oxalated blood of sensitized subjects on a glass slide In a positive test agglutination of thrombocytes can be observed This agglutination depends on two serum factors both thermolabile The specific factor I is dialyzable through a cellophane membrane whereas the nonspecific factor II is nondialyzable and can be found in unsensitized persons Since the origin of the thrombocytes did not matter it was felt that they acted only as passive indicators

Because the above test is based on a discrete thrombo agglutination which cannot always be recognized easily it has been tried to measure a positive reaction photometrically with the aid of a sensitive nephelometer With this method it became possible to visualize even slight turbidity in the plasma as well as in the serum of sensitized persons after addition of the allergen in proper dilution The previously mentioned factor I and II are responsible for this reaction Serum factor III was found to be the cause for inactivation of factor I in about 6 8 hours after the blood was drawn Factor III has two components one blocks factor II specifically and the other neutralizes the respective allergen

The author tried the nephelometric reaction on 22 patients with drug allergies In 19 the responsible drug was determined with certainty However the nephelometric reaction with the corresponding substance was positive only in 1 patient who had severe Pyramidon® hypersensitivity Th

Schw med Wchschr 88 9 6 Sep 1958

even fatal complications from such treatment Even when the dose of arsenic is carefully controlled the physician cannot be sure how much exposure to it has occurred in a patient in the past

It has been the routine practice of dermatologists to follow arsenical keratoses to detect signs of cutaneous malignancy In view of the possibility of internal carcinoma or liver damage internists also should follow such patients regularly with liver function tests chest films and gastrointestinal series Even if only an occasional case of cirrhosis or early carcinoma is detected the trouble would be worth taking It might also lead to discovery of more cases unreported or never coming to autopsy, and bring forward more evidence of the carcinogenic action of arsenic

► [The evidence that the internal carcinomas in these 2 cases were a consequence of the arsenic ingestion is not conclusive Over the years literally hundreds and thousands of patients who have received arsenical therapy have been examined for various skin lesions resulting from such treatment If internal carcinomas were definitely associated with the previous administration of arsenicals one would expect that many more cases of carcinoma of internal organs would have reported in the past Nonetheless we agree that physicians should be highly suspicious of internal carcinoma when elderly patients in particular present dermatologic evidences of chronic arsenic damage —Eds]

Blood Boron Levels in Human Infants In 34 infants and young children under treatment for various skin disorders and exposed only to dietary boron Russell S Fisher and Henry C Freimuth[6] (Univ of Maryland) found the average blood boron concentration to be 0 25 µg /ml The highest level was 1 25 µg In 37 patients exposed to boron containing medications as well as dietary boron the average blood boron concentration was 0 2 µg /ml and the highest level was 1 25 µg These levels are not significantly different from those of the first group One patient in the latter group had been given baths in boric acid solution 3 times a day for a week

Two children who accidentally received a boric acid solution orally showed blood boric acid levels of 7 89 and 7 44 mg /100 ml respectively The amount shared by the 2 children was 5 oz containing 1½ teaspoonfuls of boric acid Both children had gastric lavage at the hospital Neither exhibited any signs of boric acid toxicity at any time though these levels are above those previously reported as fatal In

(6) J Invest Dermat 30 85 86 February 1958

greater in men (14%) than in women (5%) Men with both basal and squamous cell carcinomas had a greater chance of having a second squamous cell lesion than either men or women with only a single squamous cell carcinoma These differences were not statistically significant

Of the total of 413 patients 70% were men Among patients with lesions only on exposed body surfaces 73 2% were men whereas among patients with lesions only on unexposed surfaces 53 3% were men These observations are consistent with the concept that the frequency of skin cancer is higher in men than it is in women as a result of environmental factors

► [The incidence of approximately 3% for metastasis of squamous cell epitheliomas seems somewhat high to us Roswell Park Memorial Institute is known as a cancer hospital and this may account for a high census of patients who have old invasive and therefore metastatic lesions of this type

According to the authors the chances of metastases occurring after the treatment of prickle cell epitheliomas are very small if they have not occurred within 3 years This is highly important from the follow up view point Follow up is a must for 3 years and is desirable but not likely to yield positive findings thereafter

The differences in the incidence of carcinoma of the exposed skin surface of men as compared with women are notable The principal environmental factor producing the higher incidence in men is likely to be exposure to sunlight This indicates once more how unjustified it is at present to attempt to induce people to increase their tanning via increased exposures to sunlight after taking 8 methoxypsoralen tablets —Ed]

Basal Cell Carcinoma in Children Harold L Stein and George V Webster[9] (Univ of California Los Angeles) report 3 cases occurring before age 15 Case 1 is described here

Girl 11 had discoloration of the right ala since age 6 weeks At age 5 the area enlarged and was treated with radium At age 10 skin planing was attempted and finally biopsy was performed Diagnosis was basal cell carcinoma Under general anesthesia the lesion was widely excised and a full thickness postauricular skin graft was applied to the defect The pathologic specimen showed typical basal cell carcinoma excised with adequate margins There was no recurrence during 8 months of follow up

Although basal cell carcinoma is uncommon in children it is probably more prevalent than generally realized It is estimated that 0 5 1% of basal cell carcinoma occurs before age 15 Prompt biopsy of all suspicious skin lesions in children and appropriate excision and plastic repair are recommended before the lesion progresses to wide destruction Surgery provides a specimen that the pathologist can exam

(9) Am J S 96 445-447 September 1958.

others gave negative or occasional positive reactions which on repetition were regularly negative and thus cannot b considered as true positive

The reactions with serums of patients who had eczema inhalation allergies or sensitivity to Trichophytin were always negative

► [The difference between the positive findings of Hoigne and Storck and the almost negative findings of Ziegler will have to be resolved through further studies with the nephelometric method —Eds]

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5 CANCERS PRECANCERS OTHER TUMORS AND NEVI

Frequency and Risk of Metastases in Squamous Cell Carcinoma of Skin Alfred D Katz Frederick Urbach and Abraham M Lilienfeld[8] (Roswell Park Mem I Inst Buffalo) investigated 413 patients with 601 squamous cell carcinomas of the skin during 1946 50 Lesions of the vermilion border of the lip were not counted in the total Patients with metastatic disease at admission (20 patients with 24 lesions) were not included in the calculation of the risk of metastasis The other 393 patients had 577 lesions 15 (2 6%) of which metastasized during a follow up of 5 years or more

In determining the probability of development of metastases the life table technic was used With this method the varying periods during which the patients were followed could be taken into account The probability that men with primary squamous cell carcinoma of the skin would have metastases was found to be 3 6% at the end of the 3d year and did not increase thereafter with time In women the probability was 3% Men with both squamous and basal cell carcinomas had a probability that metastases would develop that was lower (2 6%) than that for men with squamous cell carcinoma only The degree of difference was not statistically significant No essential differences based on the sites involved were noted in the proportions of lesions that metastasized

The probability that a patient with a primary squamous cell carcinoma of the skin would acquire further lesions was

(8) Cancer 10 116 1166 Nov Dec 195

All ebaceous cysts surgically removed for whatever reason should be microscopically analyzed In all older patients who have long standing cysts with recent change or a history of previous cancer the cyst should be promptly and widely excised

► [The incidence of malignancy in sebaceous cysts as reported in the literature varies greatly If it is correct that these lesions are malignant in 3 5% of the cases then they hould be treated with caution because of their potential to undergo malignant degeneration —Eds]

Investigation of Possible Apocrine Gland Component in Basal Cell Epithelioma is reported by Margaret Gray Wood Kachorn Pranich and Herman Beerman[2] (Univ of Pennsylvania) The piliary system the pilosebaceous anlage or primary epithelial germ often have been described as the source of basal cell epithelioma If basal cell epitheliomas may only develop from primary epithelial germ rather than from pluripotential cells in the epithelial or follicular basal cell layer the glandular tissue in the tumor if any morphologic or functional differentiation occurs should show characteristics common to the apocrine gland Conversely if pluripotential cells are the ancestors of basal cell epithelioma any functional or developmental characteristics of a glandlike nature might be either eccrine or apocrine

Functional or morphologic evidence of an apocrine gland component was sought by examination of 210 basal cell epitheliomas In only 2 tumor was a cystic structure suggestive of apocrine gland morphology demonstrable In both instances the structure was located deep in the tumor Morphologically the size was comparable to that of dilated apocrine glands At least part of the wall was lined with a row of cuboid cells with an outer layer of flatter cells suggestive of myoepithelial cells Small cytoplasmic buds could be seen protruding into the lumen further mimicking the appearance of apocrine glands McManus po itive material was pre ent in the stroma and formed a membrane along the external surface of the cyst No McManus positive material was found in the lumen or along the luminal surface of the epithelial cells

There is thus some morphologic evidence that these cystic structures may represent apocrine gland differentiation However examination of the cells of basal cell epitheliomas

(2) J I vest. Derma 30 273 281 J 1958

ine to establish the morphology and clearance of the margins of the lesion Radiation in children is somewhat hazardous because of the danger of arrest in growth of underlying bone The resultant scar from radiation therapy is sometimes unsightly and requires plastic revision later

► [Two cases of basal cell epitheliomas in patients under age 15 have been seen in the Oncology Section of the New York Skin and Cancer Unit during the past 4 years

One should have no difficulty guessing that this paper was written by surgeons While radiation may not be the treatment of choice for basal cell epitheliomas in children there are other simple satisfactory measures for handling such lesions e g desiccation and curettage —Eds]

Carcinoma Arising in Sebaceous Cysts Jack W Welch[1] (Hertzler Clinic Halstead Kans) reports that of 239 consecutive cutaneous cysts removed surgically and examined microscopically, 128 were benign sebaceous cysts, 6 were carcinomas with definite origin in sebaceous cysts and 106 were epidermoid cysts of which 3 were malignant The incidence of malignant degeneration of sebaceous cysts was 4 7% In distinguishing between sebaceous and epidermoid cysts histologically if the wall of the cyst showed keratinization and if a stratum granulosum could be demonstrated the cyst was considered epidermoid The sebaceous cyst is filled with sebaceous cells and debris and frequently contains large amounts of cholesterol and crystals The cyst wall is smooth and definite sebaceous cells are identifiable in it The wall is usually only a few layers thick and there is little or no keratinization

The average age of patients in this series was 64 Males predominated 2 1 Though the usual site of malignant sebaceous cysts is above the shoulder in this group 4 of 6 such cysts occurred below the neck line—3 on the thigh and 1 on the chest wall One patient had 2 malignant sebaceous cysts simultaneously Such an occurrence has not been reported previously

The longest follow up of patients in this series is 3 year and the shortest 3 months During this period there has been no evidence of recurrence or metastasis in patients with malignant cysts Since these were all cases of early carcinomatous degeneration Broders grade 1 or 2 and since all cysts were completely removed no recurrences metastases or deaths from the disease are anticipated

(1) A M A Arch Surg 76 128-137 January 1958

All sebaceous cysts surgically removed for whatever reason should be microscopically analyzed. In all older patients who have long standing cysts with recent change or a history of previous cancer the cyst should be promptly and widely excised.

► [The incidence of malignancy in sebaceous cysts as reported in the literature varies greatly. If it is correct that these lesions are malignant in 3.5% of the cases, then they should be treated with caution because of their potential to undergo malignant degeneration.—Eds.]

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Functional or morphologic evidence of an apocrine gland component was sought by examination of 210 basal cell epitheliomas. In only 2 tumors was a cystic structure suggestive of apocrine gland morphology demonstrable. In both instances the structure was located deep in the tumor. Morphologically the size was comparable to that of dilated apocrine glands. At least part of the wall was lined with a row of cuboid cells with an outer layer of flatter cells suggestive of myoepithelial cells. Small cytoplasmic buds could be seen protruding into the lumen, further mimicking the appearance of apocrine glands. McManus positive material was present in the stroma and formed a "membrane" along the external surface of the cyst. No McManus positive material was found in the lumen or along the luminal surface of the epithelial cells.

There is thus some morphologic evidence that these cystic structures may represent apocrine gland differentiation. However, examination of the cells of basal cell epitheliomas

(2) J. Invest. Derm. 30:273-281, June, 1958.

for alkaline and acid phosphatase activity and for deposits of glycogen lipid and iron revealed no positive evidence of functional activity which could be unequivocally (or even tentatively) described as characteristic of eccrine or apocrine glands

Patients with Multiple Skin Malignancies I Some Remarks on Immunobiology Observation of patients with multiple skin malignancies has offered nothing of practical value to increase their resistance to development of new tumors Leon Goldman[3] (Univ of Cincinnati) describes research being carried out in immunology in relation to skin cancer

TECHNIC—Tissue is removed with sterile precautions from a cutaneous cancer One portion is used for microscopic confirmation of diagnosis the other portion is put into a sterile container and kept in a freezer until preparation The frozen tissue is ground in a small sterile glass grinder Saline is added to the ground mass and then a modified Freund adjuvant (8 parts paraffin base Bayol F to 1 part wetting agent Arlacel) The creamy mixture is checked for sterility then used for injection Most patients are given 0 1 0 2 cc intradermally once a week for varying periods Serologic control are carried out on patients being treated

The study has been in progress for 6 months Small nodules persist for months at the site of injection but no large abscesses have developed Two instances of focal reaction in previous injection sites have been observed Progressive histologic study in these patients has shown perivascular reaction and edema suggestive of a tuberculin response Tissue eosinophilia has been observed in some sections

Studies have been carried out on 12 patients with multiple basal malignancies and 1 with multiple squamous cell tumors So far of course there has been no demonstrable effect on the active malignancies of any of the patients There is no clinical evidence that there has been any activation of any of the lesions

► [The role of immunologic factors and of host tumor relationship in malignancies is receiving increasing attention (see for example the Symposium on immunology and cancer Ann New York Acad Sc 69 525 1957) Cutaneous cancers would appear to be especially suited for investigations in this field—Eds]

Distribution of Skin Tumors of Sole of Foot M Levene[4] (Manchester England) studied the distribution of 511 lesions of the foot seen during 24 years Of 42 melanomas 25 were on the sole Almost all these lesions were on the arch

(3) J Michigan M Soc 57 551 554 Apr 1958
(4) Brit M J 1 1519 1520 June 28 1958

region of the sole and were not at sites of pressure or irrita tion due to weight bearing This suggests that much more must be learned before accepting pressure or irritation as the mechanism of spread of melanoma at least in the early stages

Squamous cell carcinomas occurred primarily on the weight bearing areas of the sole (ball of foot and heel) as did plantar warts and hyperkeratotic lesions No basal cell car cinomas were noted The incidence of squamous cell carcino ma of the foot was 1 4% of all squamous cell lesions seen at the author s hospital during the same period This low inci dence plus the fact that squamous cell carcinoma was much more common in men than in women suggests that constant trauma of weight bearing and walking may not by itself be a prime factor in carcinogenesis

Unlike other lesions angiomas of the foot often extended over wide surfaces frequently involving both the dorsum and sole Tumors arising in areas of pre existing disease were cattered indiscriminately

► [The sharp d fferences between the favored locations of melanoma and squamous cell epitheliomas are surprising In our own experience squa m us cell epitl elioma on the soles is very rare indeed. Basal cell epithe l omas of the soles are also rare but they do occur Two cases seen at the New York Skin and Cancer Unit were reported by Pascher and Sims (A M A Arch D rmat 69 475 1954) —Lds]

Skin Cancer Some Ethnic Differences Samuel D Allison and K L Wong[5] (Honolulu) report 293 cases of skin cancer seen in residents of Honolulu County by dermatologists dur ing 1955 56 The rate was 138/100 000 population for Cau casians and for non Caucasians 3 1 or a ratio of approxi mately 45 1 The difference is highly significant Differences in observed rates among various non Caucasian groups were not tatistically significant

The white population of Hawaii apparently has more ma lignant neoplasms of the skin than do white populations of elected mainland areas Whereas the rate of 138/100 000 p pulation is ba ed on reports by dermatologists only com pri ing less than 2% of physicians in the area reports in the United States from every hospital and clinic and from over ¾ of physicians indicate the rates to be 109/100 000 in Dallas 90 in San Francisco and 39 in Philadelphia

In the 293 cases reported from Honolulu County both

(5) A M A A h Derm t 76 737 739 December 1957

squamous cell and basal cell carcinomas occurred often on all parts of the body. In Hawaii physicians cannot rely on the location of lesions as an aid in determining the type.

► [Interesting figures concerning a highly important subject. Among the sources of error in these statistics are the facts that the dermatologists of Hawaii, while comprising 2% of the physicians in that area, were examining the patients with the *specific purpose* of recognizing and tabulating the various cancers of the skin, and furthermore that it is difficult to accept that every hospital and clinic and from over 94% of the physicians actually reported correctly and completely regarding cancers of the skin in the particular mainland populations under study.—Eds.]

Carcinoma in Situ of Vulva. J. Donald Woodruff and Eva E. Hildebrandt[6] report 14 cases gathered from the files of Johns Hopkins Hospital. Average age of the patients was 53; 7 were aged 50 or less and 3 were under age 40. Pruritus and/or irritation was the presenting symptom in about half the patients. A "growth" was noted by 4 patients, soreness or pain by 2. In 1, the disease was discovered on routine examination. In 6 patients ulceration was present. Two had multiple lesions. In 5, the lesions were white or leukoplakic and in 3 granular. The microscopic picture varied strikingly. Except for the hyperkeratosis in the lesions with grossly whitish appearance and parakeratosis in the granular reddened lesions, there was no definite correlation between the gross and microscopic pictures. In 3 patients vulvar disease developed after radiation therapy for cervical cancer.

Treatment in 8 patients was simple vulvectomy. One inguinal lymphadenectomy was performed due to erroneous diagnosis of invasive carcinoma. In 6 only local excision was carried out. X-ray therapy was not used. Several patients followed less than 5 years have had no recurrence. Three patients died, 2 of carcinoma of the cervix and 1 of unassociated disease.

It seems apparent from the pronounced variation in gross and microscopic appearance of carcinoma in situ of the vulva that only by careful investigation of even the smallest lesion can these early vulvar malignancies be discovered. Local excision would seem adequate in many patients. However, such intraepithelial lesions may be of multicentric origin. Consequently, simple vulvectomy with thorough study of the tissue for evidences of invasive disease would be safer.

► [Surgery of vulvar lesions should not be undertaken without benefit of

(6) Obst. & Gynec. 12:414-424, October, 1958.

a car ful histologic diagno is The decision as to what therapy should be initiated apparently presents difficulties for some physicians when vulvar changes other than malignancy are present The article by Hyman and Falk (see chapter on Miscellaneous Dermatoses) sets forth some of the errors in management which are likely to take place unless the physician can differentiate the various eruptions which may occur on the vulva and is fully acquainted with the method used in their care —Eds]

Xeroderma Pigmentosum Report of Eight Cases of Mild to Moderate Type and Course Study of Response to Various Irradiations Of the 8 patients seen by Chaim Berlin and A Tager (Tel Aviv Israel) 7 were Jews and 1 was an Arab All were dark complexioned with brown eyes and hair The face was most severely involved though other uncovered parts were not free from lesions All patients presented var ious sized freckles They appeared early in life often in un usually large numbers Their color was not uniform and varied from dark brown to coal black Dirty brown to gray brown hyperkeratotic papules 1-4 mm in size sometimes of warty or tumor like appearance covered the face from time to time Several patients presented telangiectasia and small angiomas others had leukodermic spots which had resulted from removal of tumors

One to many tumors were observed in 4 patients while they were under treatment The tumors were located on the temple eyelids nose and cheeks and grew fairly rapidly Bleeding and ulceration were often present In no instance was there evidence of involvement of regional lymph nodes

Routine laboratory examinations were normal Urinary porphyrin determinations were also normal Two patients showed moderate and 4 extreme sensitivity to ultraviolet light In 2 patients pigmentation persisted 9 months Long lasting pigmentation was also produced by 100 r filtered and unfiltered x rays and by 100 r grenz rays Therapeutic tests with corticotropin chloroquine and vitamin A showed these agents were not beneficial

► [The fact that apparently non nvolved skin of patients with xeroderma pigmentosum responds with more intense erythema and/or pigmentation following exposure to ultraviolet light x ray and grenz rays than does the skin of normal subjects leads one to speculate concerning the mechanism of these reactions Does this mean that the skin changes associated with xeroderma p gmentosum (which are considered to be precancerous) are not unl ke those that might be produced by prolonged exposure to sunlight or threshold carcinogenic doses of ion ing radiation and that exposures to only small amounts of ultraviolet light or ionizing radiation have an addi

(7) Dermat log 116 7 35 J ry 1957

tive effect thus resulting in a more intense biologic reaction clinically? —Eds]

Pre existing Roentgen Ray Dermatitis in Patients with Skin Cancer Of 105 patients with skin cancer treated by Robert S Totten Philip G Antypas S Milton Dupertuis John C Gaisford and William L White[8] (Univ of Pittsburgh) 20 gave a history of previous roentgen ray exposure All but 1 had definite clinical evidence of chronic radiodermatitis In the patient with no such evidence there were histologic radiation changes in the skin surrounding the tumor Ten patients had received radiotherapy for acne and all had basal cell carcinoma on the face neck or shoulders Three patients were physicians whose hands were exposed during repeated fluoroscopic examinations Each had squamous cell carcinoma The other 7 patients had received radiotherapy for various benign conditions (eczema psoriasis fungous and toxic goiter) Three had squamous cell tumors and 4 had basal cell carcinomas on the face neck trunk or extremities Multiple and/or recurrent tumors occurred in 9 of the 20 patients Two basal cell carcinomas were unusual widely infiltrating nonulcerating growths involving the upper lip and nose

The shortest interval between roentgen therapy and occurrence of tumor was 14 years and the mean was 25 2 years Longer follow up of patients who have had 1 000 r or less and who have been said to be without complications might reveal the occurrence of tumors even in this group

The ultimate prognosis for patients with skin cancer in pre existing roentgen ray dermatitis is probably worse than that for nonirradiated patients with similar tumors because of the high recurrence rate and the tendency for multiple tumors to develop The development of extensive tumors possibly can be reduced by careful periodic examinations early treatment of suspicious lesions and prophylactic removal of areas of radiodermatitis

► [In this study 85 of the patients with skin cancer had *not* previously received x radiation The information regarding previous exposure to x ray was obtained on history alone and *nothing* is known about the *dose* received Furthermore it is of importance to know that all but 1 of the patients with a history of roentgen radiation showed definite clinical evidence of chronic radiodermatitis

It is noteworthy that 14 of 20 patients had basal cell epitheliomas For

(8) Cancer 10 1024 1030 Sept Oct 195

merly tl e teachi ng wa that roentgen ray epitheliomas usually are of the prickl cell variety but several rece it publications reported that this i nc rrect and that basal cell epitheliomas not uncommonly arise in areas t radiodermatitis

We do n t share the authors pes mi t anticipation that epitheliomas due to fract onate l roentg n ray dose to aling le s than 1 000 r may also be foun l All evi ler ce to date suggests strongly that if one stays below that dosage and if the treatments are given ly the accepted technics no ra liodermatitis and tl erefore no epithelioma will be produced However we are afrai l that tl o e who persi t in giving much larg r total doses of fracti nated therapy for benign derma o es take a chance on producing sequelae Actually in the l ng run they may give support to tho e who object even t any use of superficial x rays in the treatment of benign d rmato es —Eds)

Adenocarcinoma of Ovary Presenting as Acanthosis Nigricans Though many cases of acanthosis nigricans and carcinoma have been reported the a sociation of this cutaneous



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di ease with primary ovarian neoplasm appears *extremely* rare L R Dingley and K H Marten[9] (King s College Hosp London) report a case

W man 50 had had no symptoms of ovarian di ease at the time he wa examined becau e of cutaneous changes A typical lesion of acantho *nigricans* was pre ent in the perianal region with thickening an l brownish l lack *di coloration of the* kin in this area The palms and the palmar surfaces of the fingers were dry coarsely hy perkeratotic (Fig 9) an l yellow Similar but less marked changes

(9) J Obs & Gy aec B t Emp 64 858 900 December 195

were present on the soles The finger nails were brittle and showed definite koilonychia The dorsal surface of the tongue was rough and granular and showed deep transverse fissuring Raised rough granular plaques were present on the inner surface of both cheeks Biopsy of the perianal lesion showed a histologic picture compatible with a diagnosis of acanthosis nigricans

No masses could be felt on abdominal palpation but some free fluid was thought to be present in the peritoneal cavity Pelvic examination revealed nodules in the pouch of Douglas At laparotomy a papilliferous cyst was found in the right ovary with metastases in the pelvis and in the para aortic and omental lymph nodes

This patient had excessive lanugo hair over the face and neck The abnormal hair growth appeared at the same time that other skin changes were first observed The authors suggest that both the acanthosis nigricans and the hair growth may represent a response to some abnormal substance produced by the ovarian carcinoma

► [Another instance in which cutaneous manifestations led to the diagnosis of internal disease Findings such as these should alert the physician to be ever mindful of the hitherto inexplicable relationship of internal carcinoma and various changes in the skin —Eds]

Malignant Melanoma of Feet and Hands According to Robert J Booher and George T Pack [1] 16 5% of all malignant melanomas noted at the Memorial Cancer Center New York from 1935 to 1950 were on the hands and feet though these surfaces constitute only 10 5% of the total body skin surface There were 29 patients with melanomas of the hands and 122 with melanomas on the feet About 60% of the lesions occurred in women All but 2 5% of the patients were white

Of the lesions on the feet 68 occurred on the dorsum and 54 on the plantar surface Only 30 lesions were apparently preceded by a mole of long standing or a birthmark Of the 122 melanomas on the feet 32 (26 2%) were treated by local excision alone with a 5 year definitive cure rate of 34 4% (11 patients) The 5 year survival rate without recurrence for all malignant melanomas of the feet was 25 3% In patients in whom groin metastases became evident during observation an average of 20 7 months elapsed before metastatic lesions were detected

In treatment of the primary lesion subungual melanomas or those on digits were removed by disarticulation at the metatarsophalangeal joint or amputation through a metatarsal bone Most of the other primary lesions were treated by

(1) Surgery 42 1084 11 1 December 1957

wide excision and immediate application of a skin graft of intermediate thickness

In radical groin dissections for proved metastases the 10 year definitive cure rate was 10 9% (5 of 46 patients) The group of elective groin dissections without clinical evidence of metastases but in which microscopic study revealed metastases yielded a 5 year definitive cure rate of 20% (1 of 5 patients) In elective groin dissections without clinical evidence of metastases and in which nodes were negative microscopically the 5 year cure rate was 40 c (4 of 10 patients)

Of all who had surgery of the feet 16 5% (20 patients) subsequently had local recurrence on the feet or widespread dissemination throughout the leg Of all who had groin dissection 25% (14 of 56 patients) had diffuse recurrence in the extremity or in the scar of the groin dissection

The 5 year definitive cure rate as compared with the diameter of the primary melanomas were 1 cm 29 4% (5 of 17 patients) 1 2 cm 20 7% (6 of 29) 2 3 cm 22 2% (2 of 9) 3 4 cm 18 1% (2 of 11) and 4 5 cm 10% (1 of 10) In 4 patients the pathologist noted vein invasion 3 of whom died of melanoma but 1 survived over 5 years without evidence of dissemination Ulceration of the primary lesion or its absence was not specifically noted often enough to consider its influence on prognosis

During 1935-47 melanomas of the feet with known metastases to the groin were usually treated by excision and skin grafting or digital amputation for the primary lesion and radical groin dissection with preservation of the leg The 5 year cure rate for melanomas so treated was never better than 14% An adequate conjoined superficial and deep groin dissection inevitably produced some blockage and lymph stasis which is the worst possible setting for residual melanoma in the leg resulting in diffuse melanomatosis by lymphatic tumor permeation Amputation after this accident has proved futile Recently melanoma of the foot has been treated by wide excision with immediate superficial groin dissection If metastases are found on frozen section analysis radical groin dissection is completed but if not the superficial groin dissection is deemed adequate

In an experimental series of 13 patients with proved groin metastases 1 patient died of melanoma over 5 years after

amputation by hip joint disarticulation combined with retroperitoneal lymph node dissection Eleven patients died in less than 5 years and 1 is living and well over 5 years after surgery The efficacy of this therapeutic approach in advanced cases remains to be proved but if the end results are to be accepted as an improvement such surgery must be done in an earlier phase of the disease than in the past

Of the 29 patients with melanoma on the hands 79.3% had lesions on the dorsal surface In 10 treatment was confined to the hand 4 (40%) of these survived 5 years The 5 year definitive cure rate for malignant melanoma metastatic to the axilla was 16.6% (1 of 6 patients)

There were 29 subungual melanomas among the total of 151 patients Two (15.4%) of 13 patients with subungual lesions on the fingers and 4 (25%) of 16 with subungual lesions on the toes had 5 year cures or more It is surprising that although melanoma of the hand carries much better prognosis in general this apparently does not hold true for subungual melanoma

► [If only the knowledge derived from the numerous statistics given in this and other papers was of sufficient help to make possible an accurate clinical diagnosis of malignant melanoma!—Eds]

Early Recognition of Melanoblastomas N Melczer and J Kiss[7] (Univ of Pecs) found that polarization resistance of the tissues the so called pseudoresistance decreases measurably at onset of malignant transformations According to the authors method with the aid of a direct current tube amplifier and microvoltmeter it is possible to determine within a few seconds and without biopsy whether a melanoma is benign or malignant This electrometric method was used in over 400 patients with epithelial skin tumors and in 1 200 patients with various more or less epithelioma like acanthomas Several thousand pigmented nevi were tested in 400 school children and in 70 adults Also studied were 14 malignant melanomas some of which were early lesions and some were fully developed 21 juvenile melanomas and 4 cases of Hutchinson s melanotic freckle

Of 465 patients with pigmented nevi (junction and compound), none showed electrometric indication of malignancy and readings were never over 4 mv Patients with juvenile melanomas also had normal readings All 14 patients with

(7) Dermatologica 117 24 5 Oct be 1958

early or late malignant melanomas 2 of whom had the achromic form had greatly reduced polarization resistance In early tumors the reading was 15 25 mv whereas in fully developed tumors the reading ranged from 20 to 40 mv Of 4 patients with melanosis circumscripta praeblastomatosa in 1 partial malignant transformation was found Biopsy after x ray treatment showed a malignant melanoma that had broken through the epidermal border

► [Methods suggested in the past for early diagnosis of malignant melanoma have failed to fulfil all of the claims made for them —Eds]

Malignant Melanoma in Albino Report of Case is presented by T Elliott Young[3] (New England Deaconess Hosp Boston) Malignant melanoma is far more frequent in light skinned races than in those with dark skin and has its highest incidence in blond persons with pale skin Despite this predilection for the light skinned person there has been no previous report of malignant melanoma in an albino

Malignant melanoma is thought to arise from the melanin producing cells of the body In the epidermis these cells have been named melanodendrocytes (Becker) In completely nonpigmented skin it might be thought that there are no melanodendrocytes and therefore that albinos do not develop malignant melanoma because of the absence of these cells However studies of nonpigmented skin by gold impregnation technics have revealed that in cases of vitiligo and albinism melanodendrocytes are present in normal numbers Dopa and tyrosinase tests are negative This suggests the nonpigmentation is due to a pathophysiologic defect in pigment production

Most pathologists make the diagnosis of malignant melanoma without recourse to special staining technics Only in amelanotic lesions without characteristic architecture such as in a metastasis are special stains required for identification of the tumor

If in an albino a tumor were to arise from these cells which are physiologically unable to produce pigment it would be anatomically identical with melanoma Because of the defect in pigment production the usual dopa and tyrosinase tests would not however be positive and the diagnosis would rest on the characteristic growth pattern

Albino Caucasian woman 40 had as the primary lesion a mole on

3 A M A Arch Path 64 186-191 Aug 19

amputation by hip joint disarticulation combined with retroperitoneal lymph node dissection. Eleven patients died in less than 5 years and 1 is living and well over 5 years after surgery. The efficacy of this therapeutic approach in advanced cases remains to be proved, but if the end results are to be accepted as an improvement, such surgery must be done in an earlier phase of the disease than in the past.

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(2) Dermatologica 117: 4-5, Oct., 1958.

Reticulosarcomatoses of Skin according to Gerd Klaus Steigleder and Hans Georg Hunscha[5] (Univ of Frankfort) embrace diseases characterized by an increase in the connective tissue cells that are not discernibly differentiated (therefore often called juvenile) These diseases are always lethal There is no primary metabolic disturbance Transitory regression of some or all skin eruptions may occur The clinical picture is variable extending from flat scaling foci to erythroderma and poikiloderma from many papules to multiple tumors The same clinical appearance does not mean the same histologic structure nor the same clinical course In the recent literature these diseases have been called reticulosis reticuloendotheliosi reticulosarcomatosis etc

Classification of the reticulo arcomatoses according to histologic structure is not feasible for a number of reasons The cells of the infiltrates have been given names on the definition of which no consensus has been reached The cells have been described according to subjective impressions This becomes especially apparent in characterization of the chromatin structure and nucleoli Unproved functional properties have been claimed for the cells Reports rarely mention the method of pretreatment of the histologic sections Staining of the nucleus and cell plasma and also the nuclear structure greatly depends on the preceding type of fixation

Mono or polymorphism of an infiltrate are not defined uniformly It has not been clearly expressed whether polymorphism in an infiltrate means a mixture of various cell type (infiltrate polymorphism) or whether it denotes the great variability of a single cell type within an infiltrate (cellular polymorphism) Infiltrations should be called monomorphic only if the variations are in one single cell type affecting size and shape It is important to remember that mutual existence of cellular elements in the same infiltrate does not mean that these elements originate from each other Recently presence of argentophil fibers has been stressed It is extremely difficult to decide whether these fibers are newly formed by the cell or whether the cells are only incidentally attached to them

It may become difficult to decide whether an infiltrate con i t of one and the same cell type or of various cell types

(5) Arch Klin exp Derm 205 435 464 1958

her calf which began to increase in size and commenced to bleed Metastases occurred to the cerebral cortex hilar and axillary lymph nodes, kidney and skin of the abdomen Dopa tests on the metastatic lesions were negative The primary lesion revealed the characteristic junctional activity and malignant nevus cells of a melanoma

► [*Unfortunately the author does not describe the clinical appearance of the mole from which the melanoma is said to have originated*—Eds]

Paget's Disease of Nipple Occurring in Young Woman Review of Literature Reports of Paget s disease of the nipple before age 30 are rare P R Joyce and J S Lekias[4] (Perth) report a case in a woman which was clinically evident at age 28, but not diagnosed until 2 years later

Woman 30 noted cracking of the nipple during the 6th month of her 4th pregnancy Treatment resulted in temporary improvement, but 2 weeks after weaning of the infant, at age 4 months cracking recurred During the next 18 months a rash appeared around the nipple and the nipple became eroded Treatment was not beneficial Examination revealed a scaly crusted eruption involving the right nipple and areola The nipple was partially destroyed There was a suggestion of a small tumor under the nipple but no deep masses or glands could be palpated Biopsy of the nipple revealed the classic changes of Paget s disease Radical mastectomy was performed Sections from several different areas of the breast parenchyma including a well defined nodule close to the axillary tail showed intraductal and early lobular carcinoma One small deposit of intraductal carcinoma was found attached to the capsule of one of the axillary nodes Paget s disease was extensive in the epidermis of the nipple and areola and at the duct orifices There was a discontinuity between the intraductal carcinoma of the breast and that present in the nipple

The histogenesis of Paget s disease of the nipple is controversial *It is generally agreed that the epidermal changes in the nipple constitute intraepithelial carcinoma* However some regard the malignant change as being of epidermal origin whereas others maintain that the carcinomatous cell are of duct origin The authors feel that Paget disease is a manifestation of mammary carcinoma which is of a diffuse type and in cases seen at an early stage is intraductal and intradermal, later to become invasive

► [*Although the histogenesis of Paget s disease of the nipple remains controversial the physician must consider any eczematous lesion of the nipple and areola as being Paget s disease until proved otherwise This does not mean that biopsy must be done in all such instances as many of these eczematous lesions will respond promptly to appropriate topical measures If however there is unsatisfactory response to treatment a proper biopsy should be performed*—Eds]

(4) Australian & New Zealand J Surg 8 45 47 Aug t 1958

Result of this study confirm the authors hypothesis that cancers may develop in fibromas This causal relation was supported in some cases by macroscopic and histologic finding cancer developing near fibroma pendulous basaloma epithelial disorganization on the surface of the fibroma and atypical epidermis In the Pinkus tumor there were premalignant lesions alongside the fibromatous structure A definite relation between fibroma and cancer also was suggested by the reported case of a planocellular epithelioma which progressed into a fibroepithelioma Premicroscopic ulcers demonstrate the existence of a premalignant or even malignant transformation The authors present experience however does not permit definite conclusions as to the value of the colposcopic method in early diagnosis of precancerous lesions of keratotic cutaneous surfaces

One important result of this study was the discovery among the 91 cases of 2 precancerous and 6 cancerous lesions These findings demonstrate that fibromas which appear clinically benign especially in regions exposed to prolonged irritation can at an advanced age be regarded as precancerous and they often reveal true malignant degeneration

Keratosis Senilis Biologic Concept of Its Pathogenesis and Diagnosis Based on Study of Normal Epidermis and 1 730 Seborrheic and Senile Keratoses is presented by Hermann Pinkus (Wayne State Univ) Keratosis senilis is a disturbance in the normal symbiosis of malpighian cells and adnexal epithelium in the epidermis The disturbed balance is believed to be due to single epidermal cells undergoing heritable changes that make them functionally inadequate increase their proliferative tendencies and through progression lead to the development of carcinoma in situ and frequently to invasive carcinoma

Examination of serial sections of typical senile keratoses and of senile skin in the vicinity of senile keratoses reveals that the epidermis has lost its granular layer and is parakeratotic The rete Malpighii consists of light staining edematous prickle cells that vary somewhat in size and shape and have lost their orderly stratified arrangement The basal layer does not usually consist of small dark staining palisade

[1] Am J Clin P h 29 193 07 M h 1958

(mono or polymorphic infiltrates) It is especially informative to compare the nucleoli found in the same infiltrate but which are subjected to various fixing fluids such as Carnoy's Maximow's or 5% formaldehyde Fixation according to Maximow and staining by Giemsa are especially useful for assessing plasma staining Poorly differentiated connective tissue cells may appear in the same or similar form in various diseases They have like the mycosis cells little differential diagnostic value

Fidner and Meyer conclude from histochemical studies that destruction alone does not prove the malignant character of reticular new formations because the same change may also be found in inflammatory diseases Steigleder and Schultis have searched for nonspecific esterase in reticulosarcomatoses and mycosis fungoides Neither the usual reactions nor by addition of or pretreatment with substance that stimulate or inhibit esterases was it possible to differentiate between reticulosarcomatoses mycosis fungoides and other specific or nonspecific infiltrations

Premicroscopic and Histologic Examination of Fibromas of Skin with Particular Reference to Their Precancerous Character T Venkei and J Sugar[6] (Budapest) report a study of 91 chronically irritated fibromatous lesions removed at the patients request for cosmetic reasons or because of susceptibility to trauma The surfaces of the lesions were stained and studied by means of Hinselmann's colposcope to discover signs indicating a precancerous or cancerous state

The lesions could be classed in three groups fibromas confirmed by histologic examination (46) histologically verified cancers (16) and lesions with histologic diagnosis of nevus benign tumor etc (29) The reason for the relatively large discrepancy between clinical and histologic diagnose (about 50%) was partly the lack or paucity of pigmentation of the nevi which therefore resembled certain semiglobular fibromas and solitary lesions observed often in benign tumors Macroscopic diagnosis of cancers resembling fibroma or developing in fibromatous terrain is not possible since the malignant portion is either a cancer at its onset or a microcancer

(6) Ann dermat 84 of (6 N Dec 19?

encies for lateral spread normal symbiosis is replaced by a labile balance between contending epithelial groups The outer surface becomes covered with keratinized adnexal squamous epithelium whereas the diseased epidermis tends to undermine and creep along the dermoepidermal junction The normal vertical succession of cells is replaced in keratosis senilis by a lateral sliding of cells over and under each other

The characteristic changes are best recognized in well developed flat scaly lesions Early changes consist of small groups of light staining irregular cells usually filling the space between two follicular ostia or bordering with sharp delineation on normal skin Advanced stages manifest a more pronounced atypical budding of anaplastic epidermis and its downward creeping around the adnexal cones which it surrounds in a cufflike pattern In some lesions the anaplastic epidermis is almost completely repressed from the open surface In these instances atypically keratinized cells may be observed in the interepithelial cleft Such lesions may resemble keratosis follicularis In some examples of keratosis senilis the epidermis becomes hyperplastic and almost verrucous and the parakeratotic layer in many piles up and may form cutaneous horns

Signs of beginning invasion which eventually lead to full blown squamous cell carcinoma are observed in three different manifestations Atypical budding of epidermis between adnexa may extend deeper and deeper and eventually involve the pars reticularis of the corium The cuffs around the adnexa may slide down farther and become invasive or the epidermis may encroach on the adnexal epithelium at the ostia thereby cutting it off from the surface

Attention directed to the pathognomonic features described and to their proper interpretation in biologic terms will result in greater accuracy in histologic diagnosis of keratosis senilis In many instances diagnosis may be made from a relatively small amount of tissue removed for biopsy if the sharply different types of epithelium in their typical relation are present Impending or accomplished progression to invasive carcinoma can also be judged with increased assurance Differentiation from other keratoses from basal cell

cells but of elements that resemble prickle cells The dermo epidermal junction may be straight and the entire epidermis relatively thin or there may be irregular buds that extend downward In other instances the epidermis may be hyperplastic and acanthotic The regular pattern of rete ridge and papillae is lost This altered anaplastic epithelium forms sharp borders against darker staining well stratified and usually somewhat hyperplastic epithelium that manifests a hypertrophic multiple granular layer and hyperkeratosis Study of serial sections reveals that the latter type of epi

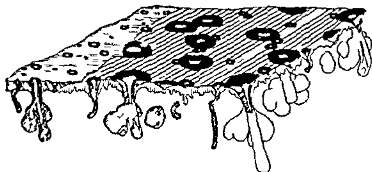


Fig 10 —Changes in keratosis senilis (Courtesy of Pinkus H Am J Clin Path 9 193 07 March 1958)

thelium always lines pilosebaceous and eccrine ostia A similarly sharp border is present at the periphery of the keratosis against the epidermis of the normal skin The dividing line is practically never vertical but is slanted with the abnormal 'native epidermis extending farther at the dermal junction and the normal adnexal epidermis farther at the keratinized surface

The biologic significance of these features is demonstrated in Figure 10 The left side represents normal epidermis Follicular and eccrine ostia are surrounded by thin tubes of adnexal epithelium The right part illustrates the concept that the epidermis in keratosis senilis has become anaplastic and biologically inadequate It is not recognized by the adnexal epithelium that begins to form epidermis as it would in the healing of wounds The adnexa build up hypertrophic inverted cones that tend to spread in an umbrella like pattern on the surface Inasmuch as the surface is not actually denuded and the anaplastic epidermis also has increased tend

nevus cell apparently came from the periphery of the original lesion

It is deduced that the original lesion appeared clinically as a completely benign common mole without a halo of pigmentation evident on examination This mole was removed by one of the common methods for cosmetic reasons Pigment recurred causing anxiety to both patient and physician Apparently when the epidermis grew over the defect it carried with it junction nevus cells which proliferated and produced the recurrent lesion and repigmentation of the area

The question of the prognostic significance of this process arise — whether this means activation of a quiescent nevus



F 11 Rec f j t (4) plet ly mov d p gm nt d i rm l vu (B) H m t yl eos d ed f om 10 (Court y of Schoen 8 H R J I F k H A M A N h D m t 8 30 3 J ly 1958)

implying possible progression to a malignant state There is no evidence of such implication in this material or that studied by Walton He found that no junctional activity occurred in any nevus which did not show it in the original lesion In none of the present cases were there any of the criteria on which the diagnosis of malignancy in a cellular nevus rest There were no mitoses no cells of unusual size and no reactive inflammatory infiltrate It seems instead that the nevus relives an early part of its natural history As in children the finding of a junction nevus is the common expected occurrence and does not imply malignant development so here in a young epidermis nevus cells form junctional nests

It is preferable to examine microscopically at least the superficial portion of nevi removed for cosmetic purposes

epithelioma and from dermatoses such as lupus erythematosus is made more easily

The principal lesion from which keratosis senilis must be distinguished is seborrheic keratosis The latter is always a cutaneous papilloma that (1) consists of well ordered epidermal cells without evidence of anaplasia and (2) manifests hyper rather than parakeratosis usually with the formation of deep keratin filled recesses or horny cysts in the substance of the hyperplastic epithelium Hair follicles and sweat ducts if they pass through the seborrheic keratosis are usually difficult to recognize because their epithelial lining is similar to the surrounding mass of cells The basal layer is well preserved and no atypical budding occurs Inflammatory reaction is often completely lacking and senile elastosis is observed only beneath lesions that occur on the exposed surfaces

► [An excellent discussion of the histologic features of senile keratoses which should prove helpful especially in cases in which it is impossible clinically to differentiate between senile and seborrheic keratoses The fact that probably 15 20% of senile keratoses undergo malignant changes makes it necessary that these lesions be evaluated carefully on the basis of clinical appearance and that all those which no longer appear quiescent be thoroughly destroyed —Eds]

Recurrence of Nevi after Incomplete Removal Robert J Schoenfeld and Hermann Pinkus[8] (Wayne State Univ) studied microscopic sections from 19 cases of recurrent pigmentation after cosmetic removal of a mole In all cases but 1 in which the original lesion was probably a wart lying near a junction nevus there were remnants of the original nevus present as nests of cells lying in the pars reticularis of the dermis (Fig 11) They showed no signs of activity and were covered with a layer of fibrous scar tissue The scar in turn was covered with regenerated epidermis showing nests of nevus cells with varying amounts of pigmentation at the dermoepidermal junction In 2 cases in which specimens of the original lesions as well as of the recurrent ones were available, the former were mature intradermal nevi with a few cell nests still present at the junction In some of the sections in which there were remaining hair roots the source of the recurrent junction nevus was thought to be nevus cells around the hair root In other sections the junction

(8) AMA Arch Dermat 8 30 35 J 1 1958

ing its high incidence in the yellow race It is seen less often in Negroes and seldom reported in Caucasians Nevertheless the authors observed 7 cases within 2 months and believe that lack of recognition is the cause of its apparent rarity

The typical clinical finding is cutaneous pigmentation accompanied by ocular pigmentation Its tonality varies and sometimes is indefinite—a mixture of brown blue and black—hence the designation brownish blue Cutaneous melanosis is usually unilateral though sometimes bilateral affecting preferentially the skin area corresponding to the 1st and 2d branches of the trigeminal zygomatic and maxillary branches a zone with a propensity for dysembrioplasias The pigmented area may be more or less homogeneous spotted or elevated it may consist of small macules separated or arranged in a network of dark color which involves particularly the inferior lid and may include the upper lid the frontoparietal region and even the nose and mouth On its surface are zones that resemble blue nevus clinically and histologically thus showing the close relation between the two dermatoses In some cases the pigmentation is found in the region of the mandibular nerve and in others follows the topography of cervical superior thoracic nerves The deep situation of pigmented elements makes therapy ineffective The lesion is benign but 2 cases of malignant degeneration have been reported

Ocular pigmentation is present in about 70% of cases It appears as slate blue round or irregular islets in the sclera There may be heterochromia of the iris because of increased pigmentation on the affected side and also pigmentation of the conjunctiva or even of the cornea Extension of ocular melanosis may produce a completely pigmented sclera Hyperpigmentation of the fundus has been reported and in some cases melanocytic infiltration may affect the extrinsic ocular muscle the retro orbital fat and even the orbital periosteum

Six of the authors 7 patients were women (In another series of 110 cases all but 22 were women) In over 50% of the present series pigmentation especially ocular was noted at birth In 1 a nasal lesion appeared at age 28 and in another at age 40 All patients were white except 1 who had a Negro great grandmother The lesion was unilateral in all Deep ocular fundus lesions were not observed and hetero

Such examination would allay any anxiety of the patient and permit recognition of the extremely rare nevus that shows histologic evidence of malignancy despite clinical quiescence as determined by an experienced dermatologist

► [These findings fit in with those of Walton Sage and Farber (A M A Arch Dermat 76 193 1957) who reported that junctional activity when present in rebiopsy specimens was histopathologically similar to that in the first biopsy The 112 rebiopsies reported by Walton *et al* and the 19 histologic examinations in the report of Schoenfeld and Pinkus of course are not sufficient to prove that in an occasional case partial removal of a nevus with junctional elements may not cause activity However the 131 biopsies in these two studies speak against the likelihood that inadequate removal of junction nevi per se is sufficient to produce transition to malignancy of a previously benign lesion —Eds]

Junction Nevus with Spontaneous Clinical Disappearance Max Braitman[9] (West New York N J) reports a case

White woman 45 had a flat, hairless pale brown plaque just below the hairline on the right side of the forehead The oral lesion had a slightly elevated border was about 1½×1 in in size and had been present for many years There had been recent increase in size Biopsy showed considerable pigment in the lower rete and basal cell layer Some of the cells were arranged in small groups The corium showed no noteworthy change Diagnosis was nevus pigmentosus (early changes of junction type)

The patient was seen by a group of dermatologists at a conference The majority opinion was to do nothing except to watch and wait. The patient reported for examination at regular intervals for 1 year and then was not heard from until 7 years later when she returned with dermatitis of the feet Examination revealed no sign of the nevus She stated that during the past few years the area had become progressively paler and flatter and had finally disappeared There had been no treatment

► [There is much evidence available at present which indicates that the junctional components of pigmented nevi undergo a gradual change and diminish over a period of years From adolescence to adulthood the junction nevus becomes a compound and finally an intradermal nevus These histopathologic change may account for the clinical differences in appearance of such lesions Perhaps this mechanism is responsible for the spontaneous disappearance of occasional lesions —Eds]

Dermo Ocular Melanocytosis (Nevus of Ota) belongs with blue nevus and Mongolian spot to the group of circumscribed congenital cutaneous melanoses characterized histologically by elongated fusiform melanogenic cells classically considered to be of mesodermal origin according to Aaron Kaminsky Jorge Dartsch and Jorge Abulafia[1] (Buenos Aires) This lesion was observed in 0 5% of all dermatologic patients at Tohoku University Japan during 1940 50 show

(9) A M A Arch Dermat 77 721 June 195

(1) Arch argent dermat 31 41 September 195

changes in Sutton's nevus in which the nevus tissue is also physiologically speaking at the periphery of the vitiligo. Vitiligo as seen here is therefore a more complex condition than vitiligo as ordinarily understood in having both a biochemical and an anatomic substratum that affects many tissue components in the dermis.

► [Sutton referred to this nevus as leukoderma acquisitum centrifugum. It has also been referred to as halo nevus and leukopigmentary nevus. —Ed.]

Centrofacial Neurodysraphic Lentiginosis, a congenital disorder characterized by lentiginous pigmentation across the nose and upper cheeks, neuropsychic changes and dysraphic manifestations, is described by A. Touraine[3] (Paris) on the basis of findings in 32 patients. Since he first described this condition in 1941 a few reports by other authors have appeared, but the condition has not received widespread attention and has been ignored in recent textbooks on dermatology.

Of the author's patients, 17 were aged 8-15, 11 were aged 17-26 and 4 were aged 30-40. The small pigmented spots, separated by healthy skin, are uniformly brown, have definite borders, are flat or slightly elevated and are localized specifically in the center of the face. The number of spots may vary from 15 to 200 or more, with the distribution somewhat butterfly shaped. In exceptional cases the spots may extend to the forehead, temples, eyelids, cheeks and chin. Two patients also had pigmented nevi on the neck and back, 2 had flat hemangiomas (lip, shoulder) and 1 had warty hairy nevi on the loin and thighs. According to the parents, the facial pigmentation appeared during the first months of life or toward the end of the 1st year. The pigmentation increased slowly until about age 8-10, then tended to decrease or disappear spontaneously. The pigmentation was not affected by light and was not more profuse in summer than in winter.

Neuropsychic disturbances were present in 29 patients. Neurologic symptoms, sometimes multiple, were noted in 6 patients (1 had infantile hemiplegia, 3 had convulsions during early infancy, 4 had epileptiform attacks). Seven showed severe mental retardation, 7 showed definitely low intelligence and 9 did poor work in school. Others showed emotional instability, temper tantrums, social maladjustment

(3) Presse méd. 66: 1611-1613, Oct. 18, 1958.

chromia of the iris was present in only 1, who also presented cutaneous lesions typical of blue nevus

Histology of Sutton's Nevus Any process which makes a cellular nevus disappear is of theoretic interest and in Sutton's nevus this sometimes happens Here a vitiliginous condition not only sometimes depigments the centrally placed nevus but may bring about its destruction This morphologic change conflicts with the prevailing view of vitiligo as a purely biochemical lesion With these problems in mind G H Findlay[*] (Univ of Pretoria) studied 8 Sutton's nevi histologically In all cases there was no other vitiligo apart from depigmentation around the nevus

Where pigment was still present in the tissue it was largely of the chromatophore type of melanin in the papillary layer of the corium Only 2 of the specimens showed a well preserved and typical nevus structure and in 1 of the e the lesion was regarded as a blue nevus In the rest varying degrees of disarrangement had taken place

The nevus cells lost their identity mainly by coarse cytoplasmic vacuolation leading either to enlargement of the cell or to collapse and crowding of the cellular material in watery spaces Cellular disintegration took place by lysis or rhexis The nevus zone itself was invaded by cells of the lymphocyte monocyte series which were often hard to distinguish from altered nevus cells Some monocytes appeared to arise by proliferation from adventitial germ centers All lesions in which cells were present were remarkable for their dense cellular packing with closed capillaries and no great intercellular edema or new fiber formation The process was sharply limited to a band of cells lying between the subpapillary layer and the upper corium above the sebaceous gland No invasive features of deeper nevus extensions were noted Fibroblastic replacement of the mass took place from below After disappearance of the cellular infiltrate the collapsed pigment free framework of the nevus consisted of a loose collagen network with some presumed increase of ground substance and dilated capillaries

The occasional case of vitiligo has been reported in which lymphoreticular proliferations have been present at the edge of the active zone These would appear to stand closest to the

(*) Brit J Dermat 69 389 394 November 1957

sels each lined with a single layer of endothelium and separated from each other and the epidermis by variable u ually very thin zones of connective tissue Treatment with repeated applications of solid car bon dioxide was not beneficial

In most in tances of keratotic hemangioma progressive development of hyperkeratosis has been noted after the ini tial angiomatous phase The lower extremities have been involved in all reported cases In Wertheim s opinion there is an actual increase in vascular elements in the area This is

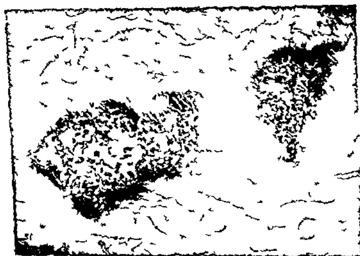


Fig 12 (Courtesy f Lor P R t J A M A A h Dermat 77 216-219 F bru ry 1958)

in contrast to the angiokeratoma described by Mibelli in which the capillaries dilate The vascular proliferation of hyperkeratotic angiomas is immediately under the epidermis whereas in angiokeratoma of Mibelli a band of connective tissue separates the vessels from the epidermis Angiokera tomas arise from preformed capillaries and are acquired le sions with a congenital predisposition but keratotic heman giomas are congenital in themselves

The authors believe that tissue asphyxia and possibly trau ma play a role in hyperkeratosis that develops in keratotic hemangiomas

defective memory, etc Dysraphic manifestations were present in 15 patients In 8 patients 14 manifestations of anterior dysraphia occurred, in 9 patients, 12 of posterior type and in 3 patients 3 of lateral type

Coexistence of centrofacial lentiginosis and neuropsychic disorders was observed in 90 6% of the patients, skin pigmentation and dysraphia in 47 1% and all three signs in 40 6% These facts indicate that presence of these various signs in the same patient is not coincidental and that this triad constitutes a specific clinical entity Its mechanism is probably as follows dysraphia probably affects the base of the skull always accompanied by gliomatosis extending toward the encephalon which accounts for the neuropsychic disorders and toward the pituitary, which accounts for the central facial pigmentation, along with possibility of an adiposogenital syndrome

Heredity is an important factor in the etiology In the families of 22 of the 32 patients on whom family history was obtained 38 instances of centrofacial lentiginosis were found In 17 families in which examinations could be carried out, 32 persons had this pigmentation In 9 families the pigmentation was found in 1 parent and in 1 or several children indicating dominant hereditary transmission There is some evidence that syphilis may play a role in causing the mutation that leads to this neuroectodermosis

► [Touraine states that this syndrome can be differentiated from the Jeghers Peutz syndrome in which similar pigmentations on the oral mucosa lips circumoral area and digits are associated with generalized intestinal polyposis —Eds]

Keratotic Hemangiomas Philip R Lorin Vincent J Derbes and John D Krafchuk[4] (New Orleans) were able to locate only 8 reported instances of keratotic hemangioma in the medical literature They report 2 additional cases

Woman 33 had 2 black elevated verrucous lesions on the anterior aspect of the right leg (Fig 12) They were elevated 3-4 mm and in their centers were superficial dry adherent scales Both lesions were indurated and painful on firm palpation They had been of lifelong duration but had become more hyperkeratotic in the past 15 years Biopsy showed a hyperkeratotic papillomatous epidermis above a diffuse zone of hemangioma in the upper dermis The epidermis showed irregular areas of hyperplasia and atrophy with numerous finger like acanthoses projecting into the dermis around hemangiomatous areas The papillae and upper dermis contained numerous dilated blood ves

(4) A M A Arch Dermat 7 216-19 February 1958

keratosis configuration in immediately adjacent areas and with minimal inflammatory changes

Likely many or most of the cases of supposed cancer arising in seborrheic keratoses reported in the literature including Sutton and Sutton's "squamous cell keratoses" were pseudoepitheliomatous hyperplasia (Weidman) in seborrheic keratoses. No unequivocal evidence was found either in a study of the present material or in a careful review of the literature to indicate that seborrheic keratoses ever give rise to actual cancer

► [We agree with Rowe that in most cases the diagnosis of seborrheic keratosis can be made without error on clinical grounds alone. When this is not the case caution should be exerted in the attempt to establish the diagnosis before such lesions are widely excised or deeply excavated on the basis of an erroneous clinical diagnosis of basal cell epithelioma, prickle cell epithelioma or malignant melanoma

We are not convinced that Rowe is correct in stating that seborrheic keratoses probably never give rise to actual cancer. Such an occurrence may be exceedingly rare but this does not mean that it never takes place. We have recently taken care of a patient with a prickle cell epithelioma which clinically seemed to arise from a seborrheic keratosis. The histopathologist who was not told of this particular feature made a diagnosis of keratosis probably seborrheic keratosis with malignant changes!—Eds]

Multiple Keratoacanthoma Report of Extensive Case and Its Response to Therapy presented by Alfred J Ephraim and Jerome J Kautman[8] (Brooklyn)

Woman 6[illegible] had about 20 dime sized lesions on the left forearm 9 years before. During the next year the lesions disappeared spontaneously leaving flat atrophic scars. Five years later new lesions appeared on the left upper arm. They were destroyed with the electric needle but new lesions appeared in some of the scars. No lesion disappeared spontaneously. During the following 3 years lesions appeared on both forearm and arm

Examination revealed round elevated hyperkeratotic and verrucous lesions varying in size from that of a dime to that of a silver dollar. The larger lesions were annular and crater like with clear atrophic white depressed centers. Biopsy showed pronounced irregular acanthosis with no invasion of the surrounding tissue. Relatively mild mostly perivascular inflammatory reaction was present. The surface was highly verrucous and covered with a tremendously increased and partly parakeratotic horny layer with no sign of anaplasia

The patient was treated with various salves and lotions without [illegible] change. A course of cortisone given for arthritis produced no improvement. However after 6 intramuscular injections of bismuth subsalicylate some improvement was noted. After 15 injections there was definite improvement especially of the larger lesions

► [The authors refer to characteristic lesions of multiple keratoacan

8. A M A Arch Dermat 7 191 194 February 1958

Seborrheic Keratoses I 'Pseudoepitheliomatous Hyperplasia (Weidman) According to Lyon Rowe[5] (Los Angeles), a surprisingly large percentage of seborrheic keratoses subjected to microscopic study have been misdiagnosed clinically Among 244 such lesions the clinical diagnosis was seborrheic keratosis in 176 nevus in 40 verruca vulgaris in 13, basal cell carcinoma in 8 senile keratosis in 2 skin tag in 3 prickle cell carcinoma in 1 and melanoma versus nevus in 1 In most instances the microscopic appearance of the misdiagnosed lesions is sufficiently suggestive of the usual picture of seborrheic keratoses to give no further difficulty Occasionally however lesions clinically seborrheic keratose or resembling some other cutaneous entity show no resemblance to a seborrheic keratosis microscopically but rather closely resemble a prickle cell carcinoma with whorls swirl and pearls of prickle cells Some of the lesions show typical seborrheic keratosis configuration in adjacent area or in subsequent biopsies

Rowe followed 3 patients clinically and with repeat partial biopsies Two had keratotic papular lesions with angiomatous elements similar to those seen in a case described by Weidman as seborrheic keratosis with pseudoepitheliomatous hyperplasia As in Weidman s case pearls and whorl were present in acanthomatous areas In 1 of the 2 patient there was no change toward malignant appearance in a 1 month interval by the usual histopathologic standards In the other the lesion showed reversion to a seborrheic keratosis with an *inflammatory cellular infiltrate The third pa*tient had a lesion clinically resembling a verrucous seborrheic keratosis or perhaps a senile keratosis From the microscopic sequence however the lesion started and ended as a serrated seborrheic keratosis of the type first described by Becker with one biopsy in between resembling the seborrheic keratosis with pseudoepitheliomatous hyperplasia Finally the lesion underwent complete involution leaving normal skin

In sections from the 244 lesions studied ample a whorl swirls and pearls of prickle cells were often found a ociated with marked inflammatory cell infiltrate in the cutis and edema and parakeratosis in the epidermis In 8 sections areas of acanthomatous change were found with typical seborrheic

(5) J Invest Dermat 1 165 180 September 195

keratosis configuration in immediately adjacent areas and with minimal inflammatory changes

Likely many or most of the cases of supposed cancer arising in seborrheic keratoses reported in the literature including Sutton and Sutton s squamous cell keratoses were pseudoepitheliomatous hyperplasia (Weidman) in seborrheic keratoses No unequivocal evidence was found either in a study of the present material or in a careful review of the literature to indicate that seborrheic keratoses ever give rise to actual cancer

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Multiple Keratoacanthoma Report of Extensive Case and Its Response to Therapy is presented by Alfred J Ephraim and Jerome J Kaufman[6] (Brooklyn)

Woman 65 had about 20 dime sized lesions on the left forearm 9 years before During the next year the lesions disappeared spontaneously leaving flat atrophic scars Five years later new lesions appeared on the left upper arm They were destroyed with the electric needle but new lesions appeared in some of the scars No lesion disappeared spontaneously During the following 3 years lesions appeared on both forearms and arm

Examination revealed round elevated hyperkeratotic and verrucous lesions varying in size from that of a dime to that of a silver dollar The larger lesions were annular and crater like with clear atrophic white depressed centers Biopsy showed pronounced irregular acanthosis with no invasion of the surrounding tissue Relatively mild mostly perivascular inflammatory reaction was present The surface was highly verrucous and covered with a tremendously increased and partly parakeratotic horny layer with no sign of anaplasia

The patient was treated with various salves and lotions without visible change A course of cortisone given for arthritis produced no improvement However after 6 intramuscular injections of bismuth subsalicylate some improvement was noted After 15 injections there was definite improvement especially of the larger lesions

► [The authors refer to characteristic lesions of multiple keratoacan

(6) A M A Arch. Dermat 77 191 194 February 1958

thoma Judging from the photographs of the lesions in the original article they are not convincingly those of keratoacanthomas They appear to be quite verrucous and present different shapes and bizarre border outlines central horny plugs are to a large degree missing and only flat atrophic scars remain after their spontaneous disappearance Even the course and the histopathologic picture are not typical for this entity—Eds]

Epithelioma Spinocellulare Segregans So called Adenoacanthoma of Sweat Glands (Lever) J Delacretaz A S Madjedi and R M Loretan[7] (Lausanne) report 15 cases in which the histologic changes described previously by Lever as adenoacanthoma of the sweat glands were observed The



Fig 13 —Local recurrence of tumor and skin metastases 1 year after treatment (Courtesy of Delacretaz J et al Hautarzt 8 51 518 November 1957)

patients (9 men and 6 women) ranged in age from 61 to 90 (average 75) The size of the tumors varied and the period of time until therapy was started ranged from 2 months to 10 years The clinical appearance varied also ulceration was noted in 7 patients a keratotic or verrucous surface in 3 and a nodular surface in 3 No pertinent data were available on 2 Local recurrence and skin metastases were observed (Fig 13) In 10 patients multiple epitheliomas or precancerous foci coexisted Lethal metastases occurred in 2 patients

Histologically, there was neoplastic proliferation of the prickle cell type The cells showed a particular generalized tendency to individual keratinization and segregation (through loss of intercellular connections) The separated cells became necrotic Subsequently cavities developed that

(7) Hautarzt 8 512 518 November 1957

contained granular cell residues The cavities were often surrounded by a single cell layer which gave them a glandular appearance The glandular character of the tumor may be apparent early when a tubular mass develops or it may develop late when cavities form progressively in the tumor Both types of development may be present in the same tumor

In none of the 15 patients were the authors able to prove a relation between the sweat glands and the tumors There fore the authors doubt the origin of adenoacanthomas from sweat gland canals as claimed by Lever They consider them to be tumors of prickle cells and propose to call them epithelioma spinocellulare segregans

Relationship between Bafverstedt s Benign Lymphadenosis of Skin and Jessner s Lymphocytic Infiltration of Skin C Postma and J Th F Sluiter[8] (Univ of Amsterdam) report a case corresponding clinically with Jessner s lymphocytic infiltration but histologically resembling benign nonfollicular lymphadenosis of the skin

Woman 34 had recurrence of skin eruption 20 times in 5 years At intervals of several week to several months one to four small round flat papules or nodules appeared on the eyelids behind the ears or on the arms The size was usually that of a pea or bean but a few times lesions about 2 cm in diameter occurred on the legs Sometimes the nodules had a narrow elevated margin and sunken center or were annular Color varied from that of normal skin to slightly reddish The lesions disappeared spontaneously after a few weeks or months The general examination and blood picture were normal In histologic preparations hyperplastic lymphatic tissue was found repeatedly There were no follicles The histologic picture remained unchanged and did not suggest a systemic affection The impression was that of lymphoreticular hyperplasia without follicular structure or reaction centers

Under the term lymphocytic infiltration of the skin Jessner and Kanof described a series of patients with recurrent papular lesions similar to those observed in the authors patient Histologically there were sharply demarcated lymphocytic foci embedded in a fine reticulum in the cutis Although Jessner Calnan and others believe that these so called lymphocytic infiltrations are not related to benign lymphadenosis of the skin (Bafverstedt) and do not resemble it the present author after careful study of the literature and prolonged observation of their patient conclude that Jessner s lymphocytic infiltration is not an independent path

(8) A t d mat en t. 38 180 188 1958

ologic picture but a variety of benign lymphadenosis of the skin In most if not all patients with benign lymphadenosis of the skin, the disease can be recognized histologically and distinguished from lymphatic leukemia

► [It would be a step backward to consider lymphocytic infiltration (Jessner) and benign lymphadenosis as being identical Lymphocytic infiltration occurs on the face chest and arms but neither Jessner nor we have observed it on the earlobes a typical localization of benign lymphadenosis The lymphocytic foci are not deep in the cutis and there is no tendency to the formation of the typical germinal centers of lymphocytomas Lymphocytic infiltration often responds to chloroquine and other antimalarial drugs but we know of no reports of such a response in lymphadenosis benigna —Eds]

Reticulohistiocytoma (Reticulohistiocytic Granuloma) is a seldom recognized but serious condition of unknown cause involving the skin often with destructive changes in the joints bones and synovial membranes accompanied by histiocytic reactions Lesions in the skin precede the destructive changes in the joints synovial membranes and bones

Hamilton Montgomery Howard F Polley and David G Pugh[9] (Mayo Clinic and Found) report 2 cases

CASE 1 —Woman 24 had nonerythematous grouped translucent discrete flesh colored to brownish round to oval papules and nodules on the face sternum arms (Fig 14) and fingers (Fig 15) Severe destructive progressive arthritis roentgenologically and clinically differing from psoriatic or rheumatoid arthritis was present Biopsy of a skin lesion showed large and giant histiocytes and no definite deposition of lipids In time the skin lesions involuted but arthritis became extremely severe and disabling

CASE 2 —Woman 59 had several soft purple raised nodules on dorsum of fingers hands and right elbow and severe destructive arthritis of the hand A specimen from the dorsum of the right forefinger revealed the typical histologic picture of reticulohistiocytoma A synovial biopsy showed large histiocytes similar to those present in the skin A similar picture was found in the bone Reactions to periodic acid Schiff and sudan black B stains were greater in the bone and synovium than in the skin (Fig 16) suggesting the presence of lipofuscin This however may have been a degenerative phenomenon and not a primary factor

Reticulohistiocytoma is not due to a disturbance in lipid metabolism in the sense that the condition can be regarded as one of the xanthomatoses The positive reaction to sudan black B explains the faint reaction encountered with sudan IV stain in the second patient and in other cases in the literature

As in the first patient cutaneous lesions in the second pa

(9) A M A Arch Dermat 77 61 7 January 1958





Fig 14 (above left) — T l t p p l o m f wom 4
Fig 15 (above) — Characteristic ha g cutaneous nodules on h g sam patient
Fig 16 (left) — Section from cutaneous les on n woman 59, h w g weakly post PAS on h t ocyt g t ll d d f m 155
(Courtesy f Montgomery H t l J.A.M.A. A h D m t 77 61 72 January 1958)

tient involuted whereas arthritic symptoms and destructive bone changes progressed Why in some patients the disease should involute spontaneously after mild arthritic changes and in other progress to mutilating and destructive changes in the joint and bone remains to be determined

Clinical Picture of Destructive Joint Changes with Multiple Reticulohistocytoma of Skin is described by Delia Walther[1] (Univ of Frankfort) with report of a case Skin change such as cutaneous and subcutaneous node have long been observed in rheumatic diseases For the past 20 year another relatively rare disease seen with a serious often destructive bone and joint disease has created wide in t re t In m t in tance it h been referred to as reticulo h ti c t ma

All reported patient presented advanced sometimes mu

[1] ll 9 81 F l m 19

tilating joint changes and skin manifestations The latter consisted of yellowish to brown red papules and nodules, pinhead to pea sized located usually on the back of the fingers and hands, joints ears head cheeks, near the nose and the neck and shoulders Similar nodes were observed on the tendon sheaths and mucous membranes The skin lesions preceded often by many years the joint lesions and later regressed spontaneously often to complete disappearance while the destructive joint changes progressed Histologically granulomas were observed in the skin which contained round cells some neutrophils eosinophils, histiocytic elements and many giant cells with 1 20 nuclei and eosinophilic homogeneous or slightly foamy plasma In the differential diagnosis xanthoma histiocytoma and granular cell myoblastoma were considered

Woman 38 had migrating rheumatic involvement of almost all joints with gradual stiffening of both hips The skin changes preceded the rheumatic involvement by several years and began with skin colored or slightly yellowish red papules on the forehead and lateral parts of the face accompanied by itching When the lesion on the face disappeared papules up to lentil size appeared on the shoulders anterior aspect of the trunk inner and extensor surfaces of the thighs and leg There were a few papules on the back of the right wrist and 3 papule on the back of the left hand

Within 1 year biopsy specimen were taken of a similar papule and examined histologically Four specimens revealed several granulomas partly in the cutis and partly in the subepidermis The epidermis appeared acanthotic and the subepidermal cutis edematous and partly metachromatic Sudan III staining revealed fat droplet in numerous cells The granuloma were surrounded by a network of thin connective tissue fiber and separated by dense bundles of collagen tissues There was cellular infiltration around the small vessels which showed thickened walls with large swollen endothelial cells often projecting into the lumen In all specimens the granulomas consisted of the same cell type Besides varying numbers of neutrophils and eosinophils there were fibrocytes and fibroblasts which often had pale bizarre nuclei and there were some large histiocytic elements which usually had 1 2 pale nuclei with vacuoles or honeycomb structure Further giant cells with dark nuclei rich in chromatin occurred in varying numbers occasionally simulating Sternberg's giant cells

The author considers the reticulohistiocytomas as manifestations of a granulomatous allergic reaction in the course of rheumatic disease

6 VESICULAR AND BULLOUS ERUPTIONS

Dyshidrosiform Eruptions and Sweat Organ I Morphologic Findings in Six Patients with Hyperhidrosis and Vesicular Eruptions of Palms and/or Soles Franz Herrmann Selma D Morrill and Marion B Sulzberger (New York Univ Post Grad Med School and Skin and Cancer Unit) investigated the possibility of whether dyshidrosiform eruptions are ever directly related to the eccrine excretory ducts and whether hyperhidrosis plays a decisive role in the pathogenesis of these eruptions

Biopsy specimens of fresh skin lesions of 6 patients with hyperhidrosis and typical dyshidrosiform eruptions (cheiropompholyx) of the palms and/or soles were studied in serial sections The excisions had to be made laterally close to the dorsal surface because the great number of sweat gland ducts would otherwise have made difficult an accurate assessment of the findings

In 2 patients a direct connection was found between the lumen of the sweat gland duct and cavity of the blister 1 of them presented the typical histopathologic findings of miliaria rubra These observations imply that hyperhidrosis is the primary factor in all these changes It seems to lead primarily to increased hydration and saturation with water of the basal corneal layer i e of the stratum compactum Presumably this swelling could cause intracorneal obstruction of the excretory ducts of the sweat glands leading to stagnation and passage of sweat and to the development of miliaria like lesions and the absorption of transepidermal water (insensible perspiration) which normally takes place in the lower stratum corneum becomes more difficult The impaired drainage leads to blister formation in the epidermis

Nosographic Position of Sneddon Wilkinson Disease among Primary Bullous Dermatoses was studied by Vittorio Mu umeci[3] (Univ of Catania) on the basis of typical clinical and histologic findings in 3 patients Differential diagnosis was possible from dermatitis herpetiformis herpes gestationis pustular bacterid pemphigus vulgaris of the bullous

(2) [illegible] 9 606 [illegible] 19 8
(3) Minerva derm 33 6 72 M[illegible] 1958

variety and Senear Usher pemphigus Although the clinical aspects suggested the possibility of Duhring's disease the latter was excluded by the histologic finding of a subcorneal bulla which is the distinctive feature in Sneddon Wilkinson disease The author questions the validity of the accepted concept of the subepidermal localization of the vesicopustular lesion in Duhring Brocq disease and advances the hypothesis that the lesion may have a subcorneal localization in this condition also

A brief review of the literature indicates that several authors (Civatte Cerutti) have suggested the possibility of a subcorneal localization of the lesion in Duhring Brocq disease Musemeci followed patients with this condition for several years Histologic studies indicated that when several lesions from various areas were examined subcorneal masses were often present and some were so large as to be true bullae In other instances the subcorneal and subepidermal bullae coexisted or were superimposed His studies confirm the coexistence of dermoepidermic lesions with subcorneal bullae in Duhring Brocq disease which Sneddon and Wilkinson believe to be strictly connected with the disease that they separated and called an entity Sneddon Wilkinson disease should not be considered a new condition and an autonomous entity but only a form of Duhring Brocq disease

Subcorneal Pustular Dermatosis (Sneddon Wilkinson) M Doglotti[4] (Univ of Turin) reports a case

Man 36 had dermatitis of 2½ year duration localized mainly in the area between the femoral condylus and the external malleolus of the left leg Morphologically the condition showed elements that were first bullous and later pustular The dermatitis was subacute afebrile and without itching characterized by periods of recovery that alternated with periods of exacerbation without evident cause and without sequelae except for moderate residual hyperpigmentation The lesion tended to heal in the center and progress peripherally with a small edge The patient's general condition was not impaired Histology showed subcorneal bulla formation filled with lymphocyte rare eosinophils and detritus of fibrin No etiologic agent was ascertained Prednisone combined with wide spectrum antibiotics brought about recovery in 15 days Earlier therapy with sulfonamides by other physicians had caused violent urticaria like reaction on large part of the skin

Clinical and histologic findings were in every respect those described by Sneddon and Wilkinson and the author had no

(4) Minerva dermat 33 3 6 March 1958

difficulty in establishing the diagnosis. The only new feature was the mode of therapy. This condition should be considered a clinical entity completely separate from those that have similar morphologic aspects. Although Duhring-Brocq disease shows objective and subjective findings common to subcorneal pustular dermatitis, the histologic finding of a subcorneal bulla, which has been described in all cases of the latter condition reported so far, is only a casual finding in Duhring-Brocq disease.

Subcorneal Pustular Dermatosis. Charles H. Greenbaum and James B. Lee (Pennsylvania Hosp., Philadelphia) report a case corresponding in the salient features with those of Sneddon and Wilkinson.

A woman, 68, was hospitalized for a skin eruption of 3 years' duration, neck pain and generalized muscle weakness. Abnormal physical findings were limited to the skin and mucous membranes. There were grouped vesicles and pustules arranged over the abdomen, buttocks and lower back in a girdle-like fashion and grouped lesions in the axillae and inframammary area. The early lesions were pinhead-sized vesicles arranged in groups, with a surrounding area of erythema. Pustules of the same size were present, some with umbilicated centers. There were also many hyperpigmented areas on the skin of the abdomen and axillae and 2 bluish vesicles in the oral cavity. Partially healed carbuncles were situated at the right hairline posteriorly and at the right upper sternum.

A biopsy specimen of the skin showed a superficial subcorneal vesicle containing neutrophils and protein precipitate, with neutrophil extension to the dermis and neighboring epidermis. There was *mild* spongiosis of the epidermis and mild perivascular lymphocytic and plasma cell infiltration of the *corium*.

With 1 Gm. chloramphenicol daily and warm saline soaks, the carbuncles healed rapidly and completely. Coincidentally, there was *resolution* of the vesicular and pustular eruption. No new lesions appeared after 1 week of treatment. Because of a toxic *neutropenia*, chloram*phenicol* was stopped after *12* days and 1 Gm. novobiocin daily was started. The patient was discharged improved *22* days after admission.

Subcorneal pustular dermatosis is a disease seen mostly in *middle-aged* women, characterized by sterile pustules and vesicles occurring in groups and singly, with a predilection *for the axillae*, girdle region and flexor areas. Patients are in *good general health*, with little or no discomfort. The pustules *are filled with* neutrophils and debris. Whether subcorneal pustular dermatosis is a separate entity or an

15 A.M.A. Arch. Derm. 77:512-515, May, 1958.

variety and Senear Usher pemphigus Although the clinical aspects suggested the possibility of Duhring's disease the latter was excluded by the histologic finding of a subcorneal bulla which is the distinctive feature in Sneddon Wilkinson disease The author questions the validity of the accepted concept of the subepidermal localization of the vesicopustular lesion in Duhring Brocq disease and advances the hypothesis that the lesion may have a subcorneal localization in this condition also

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(4) Minerva dermat 33 73 6 March 19[illegible]

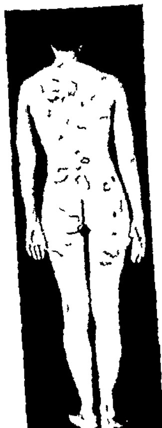


Fig [illegible] S[illegible] be[illegible] [illegible] Fig 2 [illegible] figu tion [illegible] ten [illegible] exten[illegible] Face [illegible] low part [illegible] essen[illegible]lly [illegible] The [illegible] small (some [illegible] 45 mm) [illegible] feat[illegible] (Court[illegible] of Ell[illegible] A.M.A. Arch Derma[illegible] 8 583-588 November 19[illegible])

penicillin and tetracycline as does impetigo The vesicles of dermatitis herpetiformis erythema multiforme and bullous pemphigoid are characteristically subepidermal and can be readily distinguished from the subcorneal vesicles

► [In some cases of pemphigus the vesicle or bulla is interpreted to be subepidermal instead of intraepidermal In some cases of dermatitis herpetiformis perhaps the vesicle or bulla forms subcorneally or intraepidermally instead of subepidermally

uncommon variant of dermatitis herpetiformis is unknown. If they are the same disease, the present concept of the histologic characteristics of dermatitis herpetiformis will have to be revised.

Subcorneal Pustular Dermatosis is a term used to describe patients with clinical features that are almost identical with dermatitis herpetiformis, but in which the subcorneal vesicles are virtually indistinguishable from those of impetigo. Francis A. Ellis[6] (Johns Hopkins Univ.) reports 3 cases and reviews data on 11 cases in the literature. The characteristics of the 14 cases are remarkably constant and much like those originally reported by Sneddon and Wilkinson.

The disorder is encountered primarily in women over age 40. It is characterized by superficial vesicopustules, which form annular or gyrate plaques with irregular spreading borders (Fig. 17). The lesions are located primarily on the torso and upper parts of the extremities, involving the intertriginous areas about the breasts, axillae and groin. The lesions involute to form thin superficial crusts, followed by residual hyperpigmentation without atrophy. The lesions recur in overlapping waves of healing and persist over a number of years. Local and systemic antibiotics are not helpful, but in general response is achieved after therapy with sulfapyridine or one of the sulfones.

The histologic features include a subcorneal vesicle varying in size from 0.1 to several millimeters in diameter. The vesicle is covered by a thin keratin layer, with the base formed by the granular layer, containing a thin layer of frankly purulent material that consists of serum, leukocytes and leukocytic debris, with an occasional acantholytic cell in the base of the blister. The rete may be normal or slightly acanthotic and show minimal edema and exocytosis. The papillary and subpapillary layers may be involved, with slight edema and mild round cell infiltrate.

The clinical course in subcorneal pustular dermatosis is clearly distinguishable from that of impetigo. The disorder appears in an older age group than is usual in impetigo, the vesicles often are sterile and distribution and size of the vesicles is far more extensive than in impetigo. Subcorneal pustular dermatosis is not contagious and does not respond to

(6) A.M.A. Arch. Dermat. 8:580-588, November, 195

corneal pustular dermatosis is reported by Sneddon and Wilkinson on Characteristics of the new syndrome were described as (1) erythematopustular eruption of chronic progression (2) maintenance of general health (3) characteristic histologic picture and (4) response to diaminodiphenyl sulfone therapy Review of the literature on this syndrome and on impetigo herpetiformis (known for 70 years) along with study of 3 patients persuaded the authors that it is difficult to individualize a new syndrome among acute and chronic recurrent pustular dermatoses Confusion existing with regard to the three principal types pustular psoriasis acrodermatitis continua and impetigo herpetiformis may be dissipated only by accurate etiologic information or by exhaustive study of a large series of cases Until knowledge of these conditions is more complete the general term recurrent pustuloses is preferred for all patients in whom more specific diagnosis is questionable

Case 1—Woman 39 had chronic pustular eruption for 12 years which had been interrupted by many acute episodes at first accompanied by mild fever Exacerbation of cutaneous lesions occurred predominantly during premenstrual period The patient also had lesions of the scalp eyebrows buccal mucosa and nail In one attack cutaneous lesions were accompanied by nodular lesions on the legs which might be diagnosed as nodular vascularitis

Case 2—Man 45 had cutaneous lesions similar to those of the patient in Case 1 which had progressed for 15 years At first the eruption may have been eczematiform but at time of examination the eruptions were definitely pustular High fever accompanied one of these attacks

Case 3—Man 40 had eruption of 6 months duration similar to that of the patients in Cases 1 and 2 Besides cutaneous symptoms hairy regions were involved along with axillary and posterior cervical adenopathy He had several chills but never had checked the temperature Great improvement occurred with use of diaminodiphenyl sulfone 0 mg daily with practical cure occurring within 3 weeks

The patients in Cases 1 and 3 showed clinical signs of figurate generalized aphthosis Besides the nodular and mucous membrane lesions as in the patient in Case 1 both had lesions in hairy areas and the patient in Case 3 also had small punctiform scars and localization of lesions in seborrheic region

Criteria for Histopathologic Diagnosis of Dermatitis Herpetiformis (Duhring s Disease) and Erythema Multiforme J Lerard Ad Dupont and A Fontaine[8] studied the lesions

[8] [illegible]

Dermatitis herpetiformis subcorneal pustular dermatosis of Sneddon and Wilkinson and some cases of grouped pustular eruptions of the palm and soles have in common a favorable response to sulfapyridine and certain other sulfonamides and sulfones Perhaps the common response is due to the fact that these three dermatoses are variants of the same disease process —Eds]

Subcorneal Pustular Dermatosis Report of Case is presented by Robert J Schoenfeld (Wayne State Univ)

Woman 63 Negro had recurrent generalized skin eruption of 20 years duration The abdomen scalp distal parts of extensor surfaces of the upper extremities and most of the lower extremities were covered with superficial flaccid fragile dome shaped bullae 0 5 1 cm in diameter and filled with turbid fluid Many of the lesions had opened dried and were exfoliating but no denuded areas were present There was hyperpigmentation at sites of previous lesions Nikolsky's sign *was absent and there were no oral or mucocutaneous lesions* Acute exacerbations lasting 10 14 days alternated with longer periods in which the eruption was chronic and less extensive *Biopsy* of a lesion on the arm showed acanthosis of the epidermis The stratum corneum was lifted off the space beneath it was filled with coagulated serum and leukocytes No micro organisms were noted Some leukocytes and eosinophils were noted migrating through the epidermis which was *not particularly edematous and showed no acantholysis There were* some leukocytes in and around blood vessels in the cutis but no other remarkable evidence of inflammation

The patient improved rapidly on a regimen of $KMnO_4$ bath chloramphenicol 250 mg 4 times daily and diphenhydramine hydrochloride 50 mg 4 times daily Two weeks later slight exacerbation cleared in 1 week without specific therapy but a few lesions continued *to form at irregular interval The lesions disappeared* for several weeks while treatment with prednisolone 5 mg 3 times daily was given Therapy with sulfapyridine 0 5 Gm 3 time daily produced a remission for 2 months

The lesions of subcorneal pustular dermatosis are extremely superficial vesicles that proceed to superficial scaling They may or may not show grouping often affecting the extremities but may be generalized The lesions tend to recur though response to treatment is prompt and remissions may last months They resolve with hyperpigmentation and are extremely pruritic General health is not affected Histologically the bulla is like that of impetigo contagiosa but it is sterile Until more cases can be studied the disease should be considered an entity separate from dermatitis herpetiformis which it resembles in many ways

Recurrent Pustuloses were studied by X Vilanova and J Pinol Aguade[8] (Barcelona Spain) with reference to the sub

(7) A M A Arch Derm ... 4 8 ... November 1958
(8) Pre se méd 66 149 1499 Oct 1 1958

is variably elevated in patients with pemphigus as compared with normal subjects. Plasma fibrinolysin tends to be higher in the presence of increased numbers of crusted and/or bullous lesions in the skin. In bullous disease there is some evidence of an inverse ratio between activator and plasma fibrinolysin levels. There is no apparent correlation between inhibitor and fibrinolysin levels in the patient with pemphigus or in control group.

The authors believe that the increase in proteolytic activity in patients with pemphigus is primary in the skin rather than in the plasma. The low blister thresholds in these patients may indicate that the skin is already the site of increased proteolytic activity. Moreover a low blister threshold was observed in an area of localized (vulvar) pemphigus associated with a normal blister threshold in a distant site, suggesting a local cutaneous rather than a systemic origin for the increased proteolytic activity. If this is the case, the increase in plasma fibrinolysin observed in patients with pemphigus may result from absorption of skin protease into the plasma. Present methods of identification of plasma fibrinolysin do not exclude possible augmentation from cutaneous absorption.

Adrenocortical Dysfunction in Early Stage of Pemphigus Vulgaris. H. A. Cohen, T. D. Ullmann and A. Dostrovsky[1] (Hebrew Univ. Hadassah Med. School) studied 13 patients with pemphigus vulgaris and 14 control subjects, including 8 with dermatitis herpetiformis. Patients with pemphigus all had the disease in its early stage, with only a few skin or mucous membrane lesions. Diagnosis in all patients with bullous eruptions was based on histologic examination of at least two different lesions. The following tests were performed to evaluate adrenocortical function: (1) salt tolerance test before and after administration of 10 mg. desoxycorticosterone acetate; (2) Robinson-Power and Kepler test; (3) Thorn 4 hour ACTH test and (4) 24 hour excretion of 17-ketosteroids in the urine.

It is well known that the salt retention caused by desoxycorticosterone acetate is pronounced in patients with definite adrenocortical insufficiency and those with the clinical features of Addison's disease. But in patients with only slight

[1] J. I… Derma. 30: 97-10, Apr. 1 195

layer was broken in many areas, presenting lakes of pus. The same lesions were found on the scalp. The nails also were involved.

Histologic examination showed huge intracorneal pustules with extremely acanthotic epidermis. The epithelial cells were disrupted by edema and migrating cells. In the upper cutis around the vessels was an infiltrate consisting of macrophages, lymphocytes and cells with segmented nuclei. The vessels contained many eosinophils. The entrance to the follicles contained large parakeratotic horny masses. In other sections, normal keratin layers alternated with pustules.

Serum calcium was 6.4 and 7.6 mg./100 ml. (normal 9-11 mg./100 ml.). Eosinophilia was 12.20%. The pustule content grew staphylococci. On A.T. 10 (total 32 cc.) and calcium tablets, the lesions subsided within 3 weeks and the serum calcium level became normal. Histologic studies after 14 days of A.T. 10 treatment revealed heavy parakeratotic, partly basophil horny layers covering a moderately acanthotic epidermis. The papillary vessels were extremely dilated. Around the superficial vessels, especially in the subpapillary layer, there was minimal lymphocytic histiocytic infiltration.

About 18 months later, after febrile tonsillitis, tetanic attacks recurred, accompanied by pustules on the trunk and limbs. On vitamin D_2 and calcium tablets, the skin lesions regressed within 3 weeks.

The healing stage was similar morphologically to psoriasis and could not be distinguished from it histologically. There are, however, certain differences between the two entities. Impetigo herpetiformis develops only in hypocalcemia, which is the sequela of parathyroid hormone deficiency or due to disturbances in calcium metabolism during pregnancy. Lack of calcium appears to be the cause of impetigo herpetiformis because it promptly subsides on A.T. 10. These characteristics distinguish impetigo herpetiformis from psoriasis vulgaris, pustular psoriasis and from Hallopeau's acrodermatitis as an independent entity.

► [Apparently there is no uniformity in the finding of hypoparathyroidism in all cases diagnosed as impetigo herpetiformis. The therapeutic effectiveness of A.T. 10 (tachysterol, dihydrotachysterol) in some cases is well known. Other forms of therapy, including ACTH and corticosteroids, have been reported as effective. Among the many interesting features of this case are the resemblance to psoriasis in the healing phase and the 12.20% blood eosinophilia.—Ed.]

Proteolytic Activity in Pemphigus. II. Estimations in Skin and Blood. John W. Dougherty, Frank E. Cormia and Shirley Unrau (Cornell Univ.) found that a hemorrhagic vesicle can be produced regularly in human skin by intradermal injection of the proteolytic enzyme trypsin. In most patients with pemphigus vulgaris a definite reduction in blister thresholds is found. Plasma fibrinolysin (or protease)

(A.M.A. Arch. Derm. 81: 84, March, 1960)

Eventually the conjunctival sac is closed completely and the eyeball immobilized. The scar tissue presses on the lacrimal ducts causing the conjunctiva and the cornea to dry.

Usually other mucous membranes also become involved, particularly those of the oral cavity, nasopharynx, larynx and anogenital region. In more advanced cases the mucosa of the esophagus and even the lower parts of the alimentary tract may be involved. Vesicles and bullae appear on the mucosae which break easily leaving erosions. A characteristic feature is shrinking and atrophy of the mucous membranes.



Fig. 19. [illegible] typical [illegible] so-called pemphigus ocularis [illegible] (1957)

In about half the cases blisters appear on the skin. They usually have a thick, fairly strong roof, occur on unchanged skin and in some cases lead to scarring.

The author describes a clinically typical case of so-called pemphigus ocularis involving the conjunctivas (Fig. 19) and the mucosae of the mouth, nasopharynx, larynx and genitalia. In the skin there were also some recurrent bullous lesions in the skin. For comparison a case of early pemphigus vulgaris involving the conjunctiva and oral and anal mucosae is described. Diagnosis was established in the early stage of the disease by cytologic examination of smears from the mucosae. Later a typical bullous eruption appeared on the skin.

In true pemphigus, cytologic examination reveals the presence of acantholytic cells which predominate over inflam

adrenocortical deficiency a considerable spread in the results and overlapping with the findings in normal subjects may be assumed. Thus a clearcut distinction between entirely normal subjects and patients with only slight dysfunction of the adrenal cortex can hardly be made on the basis of the results of tests similar to that used in this investigation. Therefore it is of interest that whereas patients with Duhring's disease and other skin conditions showed decreases as well as increases in water and salt excretion after desoxycorticosterone acetate, resulting in an average decrease of about 29% for sodium for the whole group, none of those with pemphigus showed any increase in water and salt excretion, and the average decrease in excretion of sodium was 49%. This difference is not statistically significant because of the great personal variations, but it appears of sufficient interest to warrant further investigation.

The results of the other three procedures showed no evidence of adrenocortical dysfunction in the control subjects, but some of the test results suggested adrenocortical dysfunction in the pemphigus patients.

Deviations from normal in water and salt metabolism as suggested by this study may be a side effect of some other adrenocortical dysfunction which may be etiologically connected with pemphigus and which should be sought by other procedures such as hormone assays.

► [Although the difference might not be statistically significant, the fact that the findings in pemphigus differ from the other bullous diseases studied makes them worthy of consideration. *Perhaps there is some adrenocortical dysfunction associated with pemphigus vulgaris.*—Ed.]

Pemphigoid Mucosae: So called Pemphigus Ocularis and Its Relation to Pemphigus. According to Stefania Jablonska, *Pawel Segal, Boguslaw Milewski* and Halina Dabrowska[4] (Warsaw Med. School) the name pemphigus ocularis is inconsistent with the fact that the disease is not a true pemphigus. It is a distinct entity which, on clinical, histologic and cytologic grounds, belongs in the group of pemphigoids. The most characteristic clinical changes are those involving the eye. Initially there is a catarrhal conjunctivitis with a ropy mucoid discharge. Subsequently scarring, thickening and shrinkage of the conjunctiva appear, with adhesions running from the bulbar conjunctiva to the eyelids (Fig. 19).

(4) Acta dermat.-venereol. 37: 364 3 5 19

Of 25 000 consecutive patients with skin diseases 1 625 (6 5%) had psoriasis and 133 (0 53%) had persistent pustular eruptions of the extremities (44 of these were males) Of the 1 625 with psoriasis 35 (2%) had pustular eruptions of the extremities In 3 patients pustular psoriasis occurred in a generalized form and proved fatal after many years

The author presents excellent photographs of the three variants of chronic pustular eruption of the palms and soles in the original article

► [It is unfortunate that so little is known about the etiologic mechanism of these persistent pustular eruptions of the hands and feet We have not been impressed by the role of foci of infection. It is not clear to us why involvement of the palms and soles suggests probable emotional instability In some cases the systemic administration of the newer sulfonamides and antibiotics especially of the newer prednisolone analogues such as triamcinolone appears to be helpful We agree with Ingram however that topical therapy particularly with tar and dioxyanthranol (anthralin cignolin) is the treatment of choice —Eds]

Prospect of Psoriasis Of 918 patients with psoriasis seen during the past 5 years Ronald Church[6] (Royal Infirm Sheffield England) interviewed 546 and reviewed their histories Age at onset was predominantly 5-15 years Most severe cases began in early childhood A family history was obtained in 34 of the patients Of 116 with severe psoriasis 41 had a family history of the disease

Nearly half of 37 patients who were first seen for guttate psoriasis had had a recurrence In 50% of these an attack of tonsillitis was recorded as the precipitating cause The total incidence of rheumatoid and psoriatic arthritis was 2% which is less than the 3 1% found in the general population Pregnancy and parturition had no effect on the disease course in 14 of patients 33 became free from psoriasis and in 4 the disease became worse In 44% parturition was accompanied by relapse of psoriasis whether it had cleared during pregnancy or not

In 400 patients the disease had been present long enough to judge its course before treatment Of these 74% had never been free from psoriasis Of those who had had remissions most had been free for only 6-12 months Only 8% had been clear for 5 years or more

The response of 260 patients to treatment with tar baths and ultraviolet was good The lesions cleared completely in

6 Brit J Dermat 70 139-145 April 1958

matory cells in the smear. The presence of a single acantholytic cell is without significance. In pemphigoid eruption the cytologic picture is dominated by many inflammatory elements accompanied by more or less numerous epithelial cells which may be edematous or show other changes but no distinct acantholysis. *The name pemphigoid mucosae is suggested for so-called pemphigus ocularis.*

► [The authors refer to ocular pemphigus which ophthalmologists also call essential shrinkage of the conjunctiva. It leads to blindness but is not fatal and, as the authors pointed out, should not be confused with pemphigus vulgaris or other forms of true pemphigus and pemphigoid eruptions. —Ed.]

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7. PSORIASIS

Pustular Psoriasis. John T. Ingram (Univ. of Leeds) considers acrodermatitis continua or perstans, pustular psoriasis and pustular bacterid to be variants of one distinctive clinical entity or one particular pattern of reaction. Since these affections are four times commoner in psoriatic patients than in others, he prefers the label pustular psoriasis to cover the whole group. The eruptions appear to be combinations of eczematous and psoriatic reactions and like so many combinations owe their recalcitrance to that fact.

The real cause of these reactions is not known, though infection, trauma or toxic or emotional stress may act as precipitating factors. Histology does not help in interpretation and does not differentiate the three types of reaction. The presence or absence of staphylococci in the lakes of pus is not significant. The sites of election, the anatomic and physiologic skin peculiar to palms and soles, must be significant and suggests physiologic, probably emotional, instability. But general measures of treatment, such as antibiotic, sedative and steroid hormones, are without effect.

As with most reactions in which the epidermal component is significant, topical measures are the more valuable in treatment, though radiotherapy is of no value. Tar and a sulfonated bitumen preparation resembling ichthammol (ichthyol) or combinations of these may be beneficial but do not readily clear the affection.

(5) A.M.A. Arch. D[illegible] 314-318, M[illegible]h, 1958.

Of 25,000 consecutive patients with skin diseases 1,625 (6.5%) had psoriasis and 133 (0.53%) had persistent pustular eruption of the extremities (44 of these were males). Of the 1,625 with psoriasis 37 (2%) had pustular eruptions of the extremities. In 3 patients pustular psoriasis occurred in a generalized form and proved fatal after many years.

The author presents excellent photographs of the three variants of chronic pustular eruption of the palms and soles in the original article.

[It is unfortunate that so little is known about the etiologic mechanism of these persistent pustular eruptions of the hands and feet. We have not been impressed by the role of foci of infection. It is not clear to us why involvement of the palms and soles suggests probable emotional instability. In some cases the systemic administration of the newer sulfonamides and antibiotics, especially of the newer prednisolone analogues such as triamcinolone, appears to be helpful. We agree with Ingram, however, that topical therapy, particularly with tar and dioxyanthranol (anthralin, cignolin) is the treatment of choice.—Eds.]

Prospect of Psoriasis. Of 918 patients with psoriasis seen during the past 5 years, Ronald Church[6] (Royal Infirm., Sheffield, England) interviewed 546 and reviewed their histories. Age at onset was predominantly 5-15 years. Most severe cases began in early childhood. A family history was obtained in 34% of the patients. Of 116 with severe psoriasis, 41% had a family history of the disease.

Nearly half of 37 patients who were first seen for guttate psoriasis had had a recurrence. In 50% of these an attack of tonsillitis was recorded as the precipitating cause. The total incidence of rheumatoid and psoriatic arthritis was 2%, which is less than the 3.1% found in the general population. Pregnancy and parturition had no effect on the disease course in 14% of patients; 33% became free from psoriasis and in 21% the disease became worse. In 44% parturition was accompanied by relapse of psoriasis, whether it had cleared during pregnancy or not.

In 400 patients the disease had been present long enough to judge its course before treatment. Of these, 74% had never been free from psoriasis. Of those who had had remissions, most had been free for only 6-12 months. Only 8% had been clear for 5 years or more.

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(6) Brit. J. Dermat. 70:139-145, April, 1958.

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(5) A M A Arch Der at 314 318 Mar h 19

entire thickness of the nail resembling the nail of a seamstress Similar erosions may be seen in patients with eczema or other dermatoses and also in generalized diseases which affect the trophism of the nail but these are much more superficial do not contain friable material are often more irregular and probing does not cause pain as in true psoriasis These nonspecific lesions may be present also in a patient with psoriasis but in such case are not manifestations of true ungual psoriasis but of a trophic disturbance due to local or generalized disease

The process of formation of psoriatic erosions is of diagnostic importance these are formed in the zone of the ungual matrix and result from a true psoriatic involvement of the matrix visible in the portion of the nail occupied by the lunula It is a true psoriatic papule which begins in the epidermal layer of the matrix leading to softening of horny tissue of the lamina with a process analogous to that of cutaneous parakeratosis and in the derma to secondary reactions of capillaries The erosions thus formed proceed with distal growth of the nail toward the free edge

The psoriatic papule may also form subungually and is revealed as red points corresponding to dilated capillaries seen through the nail which retains its smooth normal surface Occasionally a matrical erosion with growth of the nail corresponds to a subungual papule giving the impression of softening and erosion through the nail but ordinarily the subungual lesion does not rise through the nail

Nardelli suggests an explanation for the different response of nails and of hair to psoriasis The nail is a product of the epidermis and participates with the rest of the skin in epidermal function and its disturbance by disease whereas hair is subject to the determining and dominant influence of the dermal papilla and remains unaffected by the psoriatic process which is essentially ectodermal

Etiology and Pathogenesis of Psoriasis Vulgaris are discussed by N Melczer and J Bodzay[8] (Univ of Pecs) The observation that the Köbner phenomenon is a part of colloidopexy and identical with the storage of electronegative vital benzidine stains in the area of skin irritations opened new avenues in the study of the pathogenesis of psoriasis

(8) H t rt 9 351 35 A t 1958

95 (37%) and improved greatly in 141 (54%). Most patients however had remissions lasting no longer than 6 months and 11.5% of those who cleared completely relapsed in 4 weeks.

The younger the age of onset and the more numerous the other affected members of the family, the more severe and persistent the disease is likely to be. Much can be done to alleviate or even clear the eruption with intensive light therapy but its effects are temporary and freedom from the disease for 5 or more years is unusual. In young patients with extensive psoriasis the disturbance caused to their whole of life justifies recommending a change to a sunnier climate.

► [The 2% incidence of arthritis in this series should be correlated with the age of the patients at the time they were examined. It appears possible that had the author compared those of his psoriasis patients who were aged 40 or over with patients in the same age group but having nonpsoriatic eruptions such as lichen planus, dermatitis herpetiformis and other dermatoses, he would have found a significantly higher incidence of arthritis among the patients with psoriasis.—Eds.]

Nail Changes in Psoriasis according to Leonardo Nardelli (Rome)[7] are of two types: (1) true ungual psoriasis with specific manifestations of this disease and (2) nonspecific atypical changes secondary to psoriasis or its complications similar to onychoses of other origins.

True psoriasis of the nails is not often the only manifestation; conversely, cases are not rare in which at the beginning of a recurrence after complete regression or at onset of extension of a discrete stationary dermatosis ungual changes may be the only manifestation; this is followed by other cutaneous manifestations. In these cases localized recurrences tend to repeat themselves in the form of the previous attack. Sometimes the patient himself discovers that changes in the nails are the first sign of an approaching recurrence. More often ungual psoriasis accompanies cutaneous lesions throughout their course and appearance of a normal ungual lamina marks the beginning of remission. The normal nail appears in the proximal portion with a smooth lunula and proceeds to grow distally. The border between psoriatic and normal nail is arched anteriorly (semilunar curve of the psoriatic nail). The most characteristic aspect of true ungual psoriasis is a punctate onychia. The ungual lamina presents a variable number of points of rounded erosion involving the

(7) Gior. ital. de mat. 93: 7/8, 1958

s ted in area where moi ture had appeared The erythema deepened in intensity for several hours then gradually faded over several days as the lesions healed In lesions destined to show a Kobner reaction variable numbers of erythematous papules persisted and acquired a recognizable psoriatic scale after 7 14 days Persistent erythema and positive Kobner reaction were not observed in areas where stripping had stopped short of producing visible moisture

On the basis of this study it appears that trauma limited to superficial vessels with extravasation of blood cells and plasma is not sufficient to cause the Kobner reaction in psoriasis Neither is stripping of the superficial layers of the stratum corneum sufficient It is not known whether epidermal damage is essential in producing the Kobner reaction by means of mechanical trauma because vascular reactions always followed epidermal injury Further investigations should be made to determine whether capillary inflammation in itself can cause the Kobner reaction

► [Undoubtedly the cause of the Kobner phenomenon in psoriasis is more than the stimulation of epidermal or dermal structures the degree of trauma must also play a role —Eds]

Psoriatic Arthritis and Elevated Erythrocyte Sedimentation Rate Most textbooks stress the difficulty of differentiating psoriatic and rheumatoid arthritis Several distinguishing features have been described Psoriatic arthropathy is said to show a predilection for joints of the terminal phalanges whereas rheumatoid arthritis seldom involves these joints [illegible] agglutination reaction is usually absent in psoriatic arthritis and present in rheumatoid arthritis Some authors have reported that the x ray appearance in psoriatic arthritis is characteristic and completely unlike that seen in rheumatoid arthritis Marked elevation of the erythrocyte sedimentation rate is considered typical of rheumatoid disease but reportedly it is only moderately elevated in psoriatic arthritis

[illegible] H Gentele P Lagerholm and N Karlin[2] (Karolinska Hosp Stockholm) report that the sedimentation rate was markedly elevated (over 100 mm) in 25% of patients with psoriatic arthritis treated during the past year Two cases are reported the diagnosis in both being borne out by the absence of carditis rheumatic nodules pre

[2] [illegible] 33 4 9 464 19

vulgaris Since the Kobner phenomenon corre pond to pexis all diseases presenting this phenomenon which have various etiologies but a common pathogenesis can be grouped under the heading of pexidermas or pexismo e Thus psoriasis vulgaris is considered as a storage di ea e i pexiderma or pexismosis

The total fat content of the psoriatic scales is about 1.8 times greater than that of the psoriatic papules This mean about 100% increase in the fat content of the scales con id ering the approximate 40% water loss which normally occur in the horny layer

In the psoriasis factitia focus the lipids accumulate in the endothelial cells of the capillaries of the superficial vascular layer as well as around them Of the lipids derived from psoriatic scales only the phospholipids caused late inflam mation when injected intracutaneously into patients with psoriasis and into healthy persons Cholesterol cholin and neutral fats were ineffective The causative phospholipid i probably lecithin

The clinical signs of psoriasis such as hyperemia infil tration and later parakeratosis are probably related to a disturbed fat metabolism of the skin caused by stored his tamine like tissue substances which liberate various inflam matory lipids

Vascular Trauma and Pathogenesis of Kobner Reaction in Psoriasis Richard P Reinertson (Nat l Inst of Health) injured the uninvolved skin of 20 patients with psoriasis in three ways (1) suction until confluent petechiae formed (2) scarification with production of superficial bleeding and (3) removal of layers of stratum corneum with cellophane tape to about the level of the granular layer or upper mal pighian layer with appearance of a moist surface A Kob ner reaction followed scarification in 7 ca es and cellophane tape stripping in 8 None of the 20 patients had a reaction in sites of superficial petechiae Mo t patients with reaction had eruptive or widespread le ions

Effects of cellophane stripping were not limited to the epidermis Shortly after the procedure localized erythema and sometimes a surrounding flare and wheal appeared The wheal and flare la ted only a few minutes but erythema per

(9) J In e t Dermat 30 83 86 Jan 1958

ated in areas where moisture had appeared. The erythema deepened in intensity for several hours, then gradually faded over several days as the lesions healed. In lesions destined to show a Kobner reaction, variable numbers of erythematous papules persisted and acquired a recognizable psoriatic scale after 7-14 days. Persistent erythema and positive Kobner reactions were not observed in areas where stripping had stopped short of producing visible moisture.

On the basis of this study it appears that trauma limited to superficial vessels with extravasation of blood cells and plasma is not sufficient to cause the Kobner reaction in psoriasis. Neither is stripping of the superficial layers of the stratum corneum sufficient. It is not known whether epidermal damage is essential in producing the Kobner reaction by means of mechanical trauma because vascular reactions always followed epidermal injury. Further investigations should be made to determine whether capillary inflammation in itself can cause the Kobner reaction.

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(1) A d m t em 1 37 459 4 4 1957

vious infections erythema nodosum and leukocytosis and the presence of normal titers, negative Rose agglutination reactions and predilection of the joint disease for the terminal phalangeal joints Electrophoretic analysis however disclosed moderately elevated alpha₂ and beta globulin fractions such as is observed in rheumatoid arthritis In both patients the skin changes and joint involvement became worse during steroid therapy This response by the joint disease is particularly interesting because steroid therapy usually is highly beneficial in rheumatoid arthritis

► [As far as we have been able to tell the arthritis in our psoriasis patients responded very well to systemic corticosteroid therapy —ru s]

Studies on Serum Lipids Proteins and Lipoproteins in Psoriasis Walker A Lea Jr Herbert H Cornish and Walter D Block (Univ of Michigan) studied 18 patients, aged 23 55 with active psoriasis and 10 normal control subjects In 4 of the psoriatics the total lipids cholesterol and phospholipids were elevated One other patient had a slightly elevated total cholesterol Although some variation from normal was found in the serum protein patterns of the patient with psoriasis there was no consistency with respect to the protein fractions affected Results of lipoprotein analyses (in 9 cases) indicated abnormalities in the S 70 400 fraction in 6 cases in the S 40 70 fraction in 5 in the S 25 40 fraction in 2 in the S 20 25 fraction in 2 and in the S 1 10 fraction in 2

Though some abnormalities were obtained in the determinations carried out in this study they were not striking The data might be interpreted to indicate that total lipid and/or total cholesterol were elevated in a significant number of psoriatics However if the lipid data are considered in connection with the serum protein and lipoprotein data and with the clinical findings a different interpretation is presented Thus the elevated lipid fractions in 5 patients with psoriasis were accompanied by an elevated beta globulin beta lipoprotein or both These changes considered together are consistent with results obtained in atherosclerotic patients If the data are further correlated with the clinical findings in the 5 patients relative to atherosclerosis diagnosis of latent or overt atherosclerosis can be substantiated in

( ) J Invest Derm t 30 181 185 Ap il 1958

each Therefore all the lipid elevations observed in this group of 18 patients with psoriasis might be accounted for on the basis of clinical findings relative to atherosclerosis The findings in this investigation yield no evidence to indicate that psoriasis is accompanied by abnormal serum lipid level

Serum Lipoproteins in Psoriasis Edward M Shapiro John M Knox and Scott Grundy[3] (Baylor Univ) carried out serum lipoprotein and serum cholesterol determinations in 9 men and 10 women with psoriasis The patients were not on special diets nor were they receiving any systemic medication for treatment of their psoriasis The serum lipoproteins were analyzed by ultracentrifuge using the method described by Gofman and associates The serum cholesterol values were measured by the method of Pearson Stern and McGavack

Results of the study revealed no increase in lipoprotein levels of either the Standard S_f 0 12 or S_f 12-400 values The mean values for these levels were slightly low as compared to the general population The serum cholesterol values for men were normal however they were slightly elevated for women

Metabolic Studies in Psoriasis Skin Potassium and Plasma Potassium Chloride and Alkaline Values during Clinical Improvement A Reinberg J Bourgeois Spinasse M Hincky and E Sidi[4] (Paris) found skin potassium levels were normal in the uninvolved skin and very high in the lesion of 20 psoriatic patients This disturbance decreased when clinical improvement occurred under treatment Plasma potassium sodium chloride and alkaline reserve were normal during the active phase of psoriasis During improvement there was a lowering of plasma potassium in 31 of 44 patients a lowering of plasma chloride in 16 of 23 and an increase of alkaline reserve in 10 of 16 The changes were statistically significant although the values remained within physiologically normal limits Plasma sodium and glucose did not vary significantly during clinical improvement In all cases clinical improvement was obtained through energetic topical therapy Internal therapy produced spotty and irregular results

(3) J Invest Derm 31 15 217 Oct 1958
(4) [illegible] pp 31 3

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( ) J Invest Der t 30 191 185 Apr 1 1958

psoriatic skin However this as well as the other biochemical disturbances described for psoriatic plaques in recent years appear to be consequences of the disease rather than part of the basic causal mechanism —Ed]

8 LUPUS ERYTHEMATOSUS DERMATOMYOSITIS SCLERODERMA

Critique of Concept of Pre L E Cell During the past 7 years France Fascher and Alexander Borota[5] (New York Univ Post Grad Med School and Skin and Cancer Unit) examined more than 1 500 samples of peripheral blood for the presence of L E cells by the technics of Haserick Mathis Moffatt Barnes or Magath Specimens were drawn from 7 0 patients with diverse cutaneous and visceral disorders and from 11 healthy volunteers Cells resembling the so called pre L E forms were found not only in systemic lupus erythematosus but also in localized and systemic conditions in cutaneous and visceral diseases in association with negative as well as positive L E tests and in the normal subjects The highest incidence 9 10 of these forms/500 normal leukocytes occurred in 2 cases of rheumatoid arthritis and in 1 of chronic discoid lupus erythematosus The average number was 2/500 leukocytes

The authors consider these cells to be decomposition forms because of their striking resemblance to decomposition forms (Abbauformen)described some years ago in the course of in vitro studies of cellular disintegration in peripheral blood without relation to the L E phenomenon A number of outstanding hematologists concurred that these forms were artefact attributable to degeneration Attention is called to the fact that there is ample time for decomposition to set in during the course of making an L E preparation since the phenomenon requires at least ½ hour and as a rule 2 or more hours for optimal development

The intensely basophilic dense homogenized nuclear material of decomposition forms appears different from the much less compact pale staining nuclear material which makes up the inclusion body of the L E cell Cytochemical studies also indicate that the two may be distinct Because of

(5) Blood 13 376-381 April, 1958

The accumulation of potassium in lesions of psoriasis is probably due to acanthosis and the abundance of young epidermal cells. It is known that any active cellular proliferation is accompanied by an increase in potassium content. In this sense the accumulation of potassium cannot be considered specific for psoriasis. But since it is generally accepted that potassium is indispensable to the anabolism of protein and carbohydrates and hence to the cell structure, it is conceivable that it plays an important role in the psoriatic lesion. It is possible that by diminishing the potassium content of psoriatic lesions their proliferating capacity may be decreased like that of any other tissue rich in potassium.

The egress of potassium ions from cells can be related to an increase in hydrogen ions in these cells, whatever the cause for this increase in hydrogen ions may be (glycolysis, direct corticosteroid action, etc.). Therefore the clinical improvement observed in patients with psoriasis may be the result, among others, of a gain in hydrogen ions and a loss in potassium ions of the involved tissues. The fact that the topically active substances in psoriasis for the most part are strong reducing agents (tars, oil of cade, chrysarobin, anthrarobin, etc.) and certain topically applied acid may be cited in support of this hypothesis. Thus the humoral changes found during clinical improvement in psoriasis could result from the local treatment and the skin changes. It is well known that hypopotassemia associated with hypochloremia and alkalosis may be associated with loss of potassium ions and gain of hydrogen ions by the tissues.

A second hypothesis should be considered, viz., that the cutaneous changes are the result of primary humoral change. The tendency toward hypopotassemia and alkalosis suggest the possibility of an increased adrenocortical secretion, particularly aldosterone. If true, sodium retention and eventually weight gain and increased blood pressure should be observed. None of the patients in the present series showed these symptoms. Furthermore, attempts at treatment by parenteral corticosteroids or ACTH failed in most of them. Aldosterone levels were not determined in these patients, and it is not known whether an increased secretion of this hormone is or is not present.

► [Another interesting biochemical difference between psoriatic and nom

able involved in leukocyte mobility chemotaxis and phago cytosis

► [It would be interesting to know the causal drug and the variety of allergic drug eruption in the 2 patients out of 11 who had a positive reaction The only drug hitherto generally accepted as producing a systemic lupus erythematosus like syndrome is hydralazine hydrochloride (Apresoline®) although similar eruptions due to hydantoin derivatives have recently been reported (see p 180) —F l]

Evaluation of Simple Precipitation Test for Systemic Lupus Erythematosus An unusual precipitate observed during the determination of serum cholesterol in a patient who later showed evidence of disseminated lupus erythematosus led Kenneth K Jones and Harry L Thompson[2] (Tucson Ariz) to the elaboration of a test for this disease

Method —Serum or plasma 0 1 ml is placed in a test tube and 2 ml of 1? p toluene sulfonic acid in glacial acetic acid is pipetted down the side of the tube The tube is shaken allowed to stand 20 minutes then reshaken If no clot or precipitate is seen or if it disappears on shaking the reaction is negative If a precipitate persists 20 minutes after shaking and standing and then disappears on reshaking the reaction is 1+ If a precipitate persists after reshaking and standing 20 minutes the reaction is 2+ If the precipitate is heavy the reaction is 3+ and if it appears as a glassy gel the reaction is 4+

Of 13 patients acutely ill with systemic lupus erythematosus 12 exhibited test reactions of 2-4+ and 1 showed a 1+ reaction Of 17 lupus erythematosus patients who were in clinical remission or whose disease was controlled by therapy 11 showed a negative reaction and 6 showed 1+ Patients who remained severely ill showed continuously elevated test results Those who responded to therapy exhibited a fall to 1+ or negative test results The reaction became more positive when an exacerbation occurred

This test was negative in 134 of 142 patients with collagen diseases other than systemic lupus and rheumatic disease Five with chronic rheumatoid arthritis and 1 with juvenile rheumatoid arthritis gave 1+ reactions whereas 1 with chronic rheumatoid and 1 with juvenile rheumatoid arthritis gave 2+ reactions The test was negative in 64 patients with various diseases including syphilis tuberculosis heart disease carcinoma and allergic dermatitis and it was negative in 65 of 66 apparently healthy persons One gave a 1+ reaction A false positive reaction was obtained in 4 patients with hepatitis (3-4+) 1 with viral hepatitis (1+) 1 with

(2) J A M A 166 14 43 8 M 19 8

these morphologic and histochemical differences it is felt that these nonspecific forms cannot be regarded as precursors of the L E cell These cells appear to have no diagnostic significance

Interaction of Nuclei and Globulin from Lupus Erythematosus Serum Demonstrated with Fluorescent Antibody Using the fluorescent antibody technic George J Friou Stuart C Finch and Katherine D Detre[6] (Yale Univ) demonstrated a globulin component with a marked affinity for nuclei in serum of patients with disseminated lupus erythematosus The factor reacts with nuclei of most tissues of many vertebrate species When serum specimens are tested simultaneously against human tissues and material from other source there is no apparent difference in brightness of the reaction indicating lack of any species specificity

Positive results were obtained with serum from 27 of 28 patients with disseminated lupus In many of these (including the 1 with negative serum) the disease was in a quiescent stage Only 9 gave positive L E tests although the L E test had been positive in all cases at some time in the past There was some variation from serum to serum in the intensity of the staining and this was consistent in repeated tests Detailed analysis could not be made of the strength of the reaction in relation to disease activity but those patient with severe active disease tended to have most marked nuclear staining and those in partial or complete remission the least

Positive reactions were observed in a few patients with disease syndromes known to be closely allied with lupus (rheumatoid arthritis scleroderma and dermatomyositis) and in 2 of 11 patients with allergic drug reactions Reaction in patients who did not have lupus erythematosus were relatively weak No reactions occurred with the serums of 44 patients with various acute and chronic disorders other than those mentioned Included in this group were serums which contained C reactive protein and heterophil antibody as well as those with various general alterations in protein fractions The authors suggest that the L E phenomenon requires participation of the factor demonstrated in this study plus vari

(6) J Immunol 80 3 4 329 April 1958

The po ibility that the L E factor is a ba ic protein can not be excluded However the following characteri tics would put the L E factor more into the group of antibodies (1) Cell nuclei loaded with the L E factor are inge ted by granulocytes (2) An experimental antinuclei erum show characteristics very simil ir to tho e of the L E erum (3) The antigenic pecificity for nuclei depend on the pre ence of nucleoprotein

Latex Agglutination Test for Disseminated Lupus Erythematosus ia de cribed by Charle L Chri tian Ricardo Mendez Bryan and Daniel C Larson[9] (Columbia Univ) Serums were obtained from 24 patient with documented di eminated lupu erythemato u 6 with probable dis eminated lupu erythemato u 4 with di coid lupus erythemato u 53 with rheumatoid arthriti and 84 with a variety of di agno e Using a modification of the F II latex fixation test polystyrene latex particles (diameter 0.81μ) were coated with calf thymus nucleoprotein Latex particle o treated were agglutinated by 19 of the 24 serums of patients with documented dis eminated lupu erythematosu Agglutination wa po itive with 2 of 6 erums of patients with probable di eminated lupu and was negative with all erums of patient with rheumatoid arthritis and miscellaneous di ease

Agglutination of nucleoprotein latex appeared to be specific for dis eminated lupus erythematosus The test correlated closely with results of L E cell preparations on the ame serum Of particular interest are the consistently *negative* results with rheumatoid arthriti erums since the incidence of positive L E cell te t in the e patients remains highly controver ial

De oxyribonucleic acid in mall amounts inhibited nucleoprotein latex agglutination Ab orption of di seminated lupus erythemato us erums with nucleoprotein latex *removed* the agglutination property and the L E cell factor Present data suggest that the serum factor which induces L E cell formation is the same a that which agglutinates nucleoprotein latex particles and that this factor reacts primarily with de oxyribonucleic acid

Some properties of the L E cell factor sugge t that it may be part of an immunologic reaction with pecificity for nu

9) Proc Soc Exper B l & Med 98 8 0 8 3 N x pt 1958

disseminated coccidioidomycosis (4+), 2 with fulminating multiple myeloma (4+) and 3 of 11 with discoid lupus erythematosus (1+)

The precipitation test seems to differentiate systemic lupus erythematosus from periarteritis nodosa scleroderma dermatomyositis and rheumatic fever and gives few false positive reactions in rheumatoid arthritis The test result can be modified to some degree e g by therapy with adrenocortical steroids or corticotropin or by a remission but it appear to parallel the progress of the disease The identity of the substance causing the precipitation is obscure

► [The value of this test for lupus erythematosus seems doubtful Lee and Schultz (J A M A 167 1552 July 19 1958) after using this test came to the conclusion that it defines a nonspecific imbalance among the serum globulins and that its specificity and sensitivity are not great enough to warrant its use as a routine diagnostic method in the disease DuBois Rosenfeld and Ohtomo (J A M A 158 813 Oct 11 1958) came to the conclusion that the test is completely nonspecific and that as a diagnostic procedure for systemic lupus erythematosus it should be abandoned —Eds]

Serology of L E Phenomenon is discussed by P Miescher[8] (Univ of Basel) Because the L E factor can be adsorbed to specific cell nuclei it became possible to detect the factor with antiglobulin consumption tests The principle of these tests is that the L E factor a gamma globulin can be taken up by cell nuclei and then liberated at 60 C The presence of the L E factor in the eluate may be demonstrated by the fact that an anti human globulin serum can be partially neutralized in its activity by addition of the eluate Cell nuclei can be loaded with the eluate However, the eluate is usually too weak for demonstration of the L E phenomenon

Using the antiglobulin consumption test the author found that the L E factor reacts specifically with cell nuclei and independently of the organ or species from which the nuclei were isolated (absent organ or species specificity) It was also observed that the L E serum can be partially or completely inactivated by saturation with nucleoprotein or desoxyribonucleic acid

The author was able to demonstrate the L E factor by passive hemagglutination when nucleoprotein or desoxyribonucleic acid was used as an "antigen" However this test is less sensitive than the antiglobulin consumption test

(8) Ha tarzt 8 50 505 November 1957

left eye Electrophoresis showed decreased serum albumin (36.2%) considerable increase of gamma globulins (44.3%) with 7.2% beta 5.1% alpha and 7.2% alpha₁ Decrease of beta₁ globulins was greater than usually seen in active lupus Antierythrocytic antibodies (before transfusions) were strongly positive especially autoagglutination of the patient's red cells (Coombs direct positive with 2 serums of different origin) agglutination of red cells sensitized by patient's serum in a hyperalbuminous solution with red cells treated by papaine cold agglutinins to human red cells were positive in 1:64 dilution Consumption of antiglobulin of red cells sensitized by patient's serum was 100% and complement was decreased to 29 units (control 50) Leukoprecipitins gave only very weakly positive results

The patient insisted on leaving the hospital when red cells had increased to 3,500,000 with 5,800 white cells She remained on cortancyl 60-80 mg./day for another month, during which temperature remained normal and hemogram was unchanged reticulocytes being reduced to 2.5% However the skin lesions over the ankles and tibial crests and the joint symptoms recurred

It is interesting that in this case the formation of Hargraves cells was particularly active at the time of active hemolysis and the presence of antibodies in the serum Whether the two phenomena are identical is a matter for future study

Hepatitis and Cirrhosis in Women with Positive Clot Tests for Lupus Erythematosus Lloyd G Bartholomew Albert B Hagedorn James C Cain and Archie H Baggenstoss (Mayo Clinic and Found.) report 7 cases All 7 patients were females 4 were under age 25 For periods of 6 months to 13 years before evidence of hepatic disease appeared these patients presented protean symptoms consistent with the clinical diagnosis of disseminated lupus erythematosus Episodic and migratory joint manifestations including pain swelling and redness were prominent in 5 patients the other 2 had significant arthralgia Recurring unexplained fever was recorded in 6 patients Typical pleuritic pain occurred in 4 Repeated examination of the urine in 6 of the 7 patients showed sporadic occurrence of albuminuria microscopic hematuria and cylindruria Five were sensitive to light or unusually susceptible to drugs Intermittent transient erythematous or urticarial eruptions were noted in 3 patients during an exacerbation of joint pains All 7 patients had anemia Although none gave a history of syphilis a positive serologic reaction for syphilis was obtained in 4 Episodes of

(2) New England J. Med. 259:947-956, Nov. 13, 1958

clear constituents. At present this remains speculative and there is no evidence that the factor is responsible for the diverse manifestations of disseminated lupus erythematosus.

Lupus Erythematosus Disseminatus and Acquired Hemolytic Anemia with Autoantibodies were observed in a patient by Jacques Debray and X. Najean[1] (Paris).

Woman 29 with a history of a rheumatic condition was hospitalized in April 1955 because of dyspnea on exertion and subfebrile attacks which had been progressing steadily for several months. She was extremely pale, had a temperature around 100.4 F., joint pain, a slight systolic murmur and moderate splenomegaly. Red cell count was 1,500,000 with 350,000 platelets, 8,600 leukocytes and 50% polynuclear cells. Serum bilirubin (80 mg.) was almost completely of indirect type. Blood smears showed 27% reticulocytes and sternal myelogram contained 61% erythroblasts, 17% of immature forms. Sedimentation rate was 120-137; fibrin did not exceed 3.65%, but there was general proteinemia of 73.5 Gm. with 45 Gm. globulin and 28.5 Gm. albumin. Pharynx showed rare beta hemolytic streptococci group A; antistreptolysin titer was 960 units in serum. All tests for hemolytic anemia were positive (Coombs direct, autoagglutination of red cells in protein saturation, autoagglutination of trypsinized red cells). Numerous Hargraves cells were found in the blood and marrow.

Cortisone (300 mg./day) reduced the temperature and some days later the joint swelling. Red cells increased to 2,600,000 early in May when her husband insisted on her leaving the hospital prematurely. She continued with the same dose of cortisone and red cells had increased to 3,200,000 by June 1. Antistreptolysin was reduced to 640 units and other hematologic tests, though still positive, showed improvement. After sudden cessation of cortisone at the beginning of July, red cells fell to 2,000,000 and tests for hemolysis were again strongly positive. She was seen briefly a few times during the following year and tests showed progression of the syndrome. Cortisone was taken irregularly and the patient's husband refused to allow her to remain in the hospital for study. Eventually she returned very ill in June 1957. Temperature had increased to 102.2-104 F. and dyspnea and pallor were extreme. The joints had remained silent, spleen was not enlarged and facial skin was normal. There was no traumatic infection or drug factor to explain the sudden decrease in red cells to 600,000 with 12,600 white cells, 69% polynuclear cells, 6% myelocytes, 89% reticulocytes and 1,700,000 platelets. There was erythroblastosis of the marrow (60%), urobilinuria (but bilirubinemia did not exceed 10 mg.) and hemoglobin was 20 mg./100 ml. Supplementary studies were made during emergency treatment (200 cc. of deplasmatized red cells daily with 60 mg. metacortandracin).

The ocular fundus showed whitish exudate in the temporal region of the right eye and temporal punctate hemorrhages with cotton wool exudate and small exudates and hemorrhages in the nasal area of the

(1) Presse méd 66 733-5 Apr 23 1958

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The patient insisted on leaving the hospital when red cells had increased to 3 00 000 with 800 white cell She remained on cortancyl 60 80 mg/day for another month during which temperature remained normal and hemogram was unchanged reticulocytes being reduced to 2.5% However the skin lesions over the ankles and tibial crest and the joint symptoms recurred

It is interesting that in this case the formation of Hargrave cells was particularly active at the time of active hemolysis and the presence of antibodies in the serum Whether the two phenomena are identical is a matter for future study

Hepatitis and Cirrhosis in Women with Positive Clot Tests for Lupus Erythematosus Lloyd G Bartholomew Albert B Hagedorn James C Cain and Archie H Baggenstoss (Mayo Clinic and Found) report 7 cases All 7 patients were females 4 were under age 25 For periods of 6 months to 13 years before evidence of hepatic disease appeared these patients presented protean symptoms consistent with the clinical diagnosis of disseminated lupus erythematosus Episodic and migratory joint manifestations including pain swelling and redness were prominent in 5 patients the other 2 had significant arthralgia Recurring unexplained fever was recorded in 6 patients Typical pleuritic pain occurred in 4 Repeated examination of the urine in 6 of the 7 patients showed sporadic occurrence of albuminuria microscopic hematuria and cylindruria Five were sensitive to light or unusually susceptible to drugs Intermittent transient erythematous or urticarial eruptions were noted in 3 patients during an exacerbation of joint pains All 7 patients had anemia Although none gave a history of syphilis a positive serologic reaction for syphilis was obtained in 4 Episodes of

(2) New Engl J Med 259 947 956 Nov 13 1958

unexplained weakness and excessive fatigability occurred in all

The recent development of jaundice or some other evidence of hepatic decompensation seemed to precipitate the terminal phase in the 4 patients who died of their systemic illness While at rest the patients had a good appetite were well nourished and showed a sense of well being belying the seriousness of their disease Spider angiomas were universally present and an easily demonstrable hepatosplenomegaly was present in most Among tests of hepatic function that gave unequivocally abnormal results were the thymol turbidity and cephalin cholesterol flocculation and determinations of serum albumin prothrombin time and serum bilirubin In all 7 patients marked hypergammaglobulinemia and extreme elevation of the sedimentation rate were present and typical cells of disseminated lupus erythematosus were repeatedly shown in the serum and bone marrow

In view of the protean nature of disseminated lupus erythematosus and its characteristic involvement of the endothelium of small blood vessels it would seem strange if it did not at times involve the vast capillary network of the liver That such involvement actually occurs is suggested by the fact that the lymphatic vessels at the hilus of the liver are dilated and increased in a number of patients with disseminated lupus erythematosus even when there is no associated ascertainable disease of the hepatic parenchyma This suggests that in disseminated lupus erythematosus marked increase in the permeability of the sinusoids leads to increased output of lymph The present patients with a clinical syndrome strongly suggestive of disseminated lupus erythematosus experienced a massive insult to the hepatic parenchyma that histologically resembled acute and subacute viral hepatitis in 5 instances and resulted in postnecrotic cirrhosis in 2 instances In view of these facts other explanation of these bizarre cases deserve consideration

Until a specific test for the virus of hepatitis is perfected the possibility that the present patients had two diseases namely disseminated lupus erythematosus and superimposed viral hepatitis cannot be completely ruled out Furthermore despite what appears to be overwhelming clinical and laboratory evidence of disseminated lupus erythematosus the possibility that the syndrome is representative of an unusual

form of primary disease of the liver must be considered

Serum Glutamic Oxalacetic Transaminase in Dermatomyositis Assessment of the degree of clinical activity of dermatomyositis is difficult because the cutaneous findings and myositis pursue their own courses with no apparent relation between the degree of activity in either Ordinary laboratory findings are not correlated with the activity of the process and even urinary creatine and creatinine excretion studies are not as reliable guides of clinical activity as was formerly presumed

Elevation of serum transaminase levels appears to be related to injury or destruction of certain tissues with release of the enzyme into the serum Serum transaminase activity has been found to be elevated in patients with muscle disease particularly dermatomyositis Jose M de Moragas Harold O Perry and Gerard A Fleisher[3] (Mayo Clinic and Found) studied serum transaminase activity in 17 patients with dermatomyositis Three patients with disease in the inactive phase had normal levels 14 with active disease had high levels that were in some cases extreme The average for 50 normal subjects was 1 01 µM /hour/ml Some patients with active dermatomyositis had levels 10 times as high In 4 patients clinical improvement was accompanied by decreasing values of the serum transaminase

Serum transaminase determinations appear to be a useful index of clinical activity in dermatomyositis and are an aid in diagnosis However the authors stress the nonspecificity of serum transaminase activity in dermatomyositis The activity may be elevated in conditions such as systemic lupus erythematosus which are considered in the differential diagnosis of dermatomyositis Normal serum transaminase levels would make a diagnosis of active dermatomyositis unlikely

► [While this test is obviously not specific for dermatomyositis it is nevertheless one more procedure which can be utilized in the differential diagnosis of this disease —Eds]

Diffuse Scleroderma Clinical Study of 65 Cases is presented by Zdenek Stava[4] (Charles Univ Prague) Acrosclerosis was present in 57 women and only 3 men whereas diffuse generalized scleroderma occurred in 2 women and 3 men Apparently diffuse scleroderma of the acrosclerotic

(3) J.A.M.A 165 1936 1938 Dec 14 1957
(4) Dermat logica 117 135-147 September 1958

type is almost exclusively a disease of women In most patients Raynaud s phenomenon occurred first between ages 20 and 30 whereas onset of sclerodermatous changes was most common between ages 30 and 40 In 30% of cases acrosclerosis occurred in women with premature menopause or marked menstrual disturbances Almost one third of married women with acrosclerosis were childless and another third had only 1 child

The common clinical findings in patients with acrosclerosis included Raynaud s phenomenon heightened perspiration mainly of the palms and feet hardening of the skin sclerodactylia masklike facies, trophic ulceration of the finger tips and over joints paronychias and trophic nail changes trophic hyperkeratoses over joints and bony prominences mutilations of the fingers hyperpigmentation telangiectasia of the face neck and even the extremities joint manifestations muscle pains and pain in the feet when walking Less common findings were sclerostomia microglossia paradentosis atrophy of the gums and alveoli decay and loss of teeth radial perioral wrinkles dysphagia headache and keratoconjunctivitis sicca

Internal x ray endocrinologic neurologic and laboratory examinations indicated that advanced acrosclerosis can actually be considered progressive systemic sclerosis In vivo this sclerosis can be proved only with difficulty in most internal organs although sclerosis of the lungs and esophagus can be demonstrated in many patients So called sclerodermatous heart disease is difficult to diagnose on the basis of the ECG In the present group in contrast to previous reports serum calcium and phosphorus levels were within normal limits Blood counts were normal but sedimentation rate and dysproteinemia increased in proportion to progression of the acrosclerosis

Prognostically it is important in acrosclerosis that the extent and degree of involvement of internal organs do not always parallel the severity of the sclerodermatous process

Raynaud s Syndrome, Acrosclerosis Scleroderma In the course of long standing Raynaud s disease sclerodermatous changes of the hands may develop which are identical with the initial stage of diffuse scleroderma According to S Ja

blonska B Bubnow and B Lukasiak[5] (Warsaw Med School) when differentiation between scleroderma like changes in Raynaud s disease and early scleroderma is difficult or impossible on clinical grounds a decisive clue may be afforded by function tests particularly by determination of sensory chronaxy of the skin

In normal conditions sensory chronaxy values vary between 0 1 and 0 6-0 8 sigma depending on the site In various skin diseases chronaxy is prolonged in the skin lesions depending on the morphologic character of the changes Only in scleroderma circum cribed as well as diffuse is it prolonged in seemingly healthy skin and in the lesions much more so than in other diseases In diffuse scleroderma chronaxy is prolonged in the lesions to 2 5 10 sigma and varies in the seemingly healthy skin between 1 5 and 7 sigma In circumscribed scleroderma the indexes are usually lower (within the foci 1 5 7 sigma and in the healthy skin 1 5 sigma) In lon standing Raynaud s disease with sclerodermatous changes in the hands clinically indistinguishable from sclerodactylia chronaxy is prolonged in the affected skin but this is of no significance since it depends only on the morphologic character of the lesion It is absolutely normal in the rest of the skin

Capillaroscopy is also of some accessory value for it reveals two entirely different pictures in Raynaud s disease and in diffuse scleroderma In Raynaud s disease the capillary loops are extremely dilated and enlarged with irregular indented outlines and aneurysmal dilatations of the walls The blood stream is slow and vascular reactions to physical stimuli are reduced In scleroderma the number of loops is substantially decreased the capillaries are markedly deformed and occasionally only parts of loops are visible The blood stream is slow and beaded with frequently visible large gap Reactions to physical stimuli are usually suppressed In cases of pseudosclerodermatous change in Raynaud s disease of long duration angiospastic changes of the arterioles over many years and proliferation of collagen obliterate the lumens of the capillaries by strangulation so some of the loops are deformed shortened and thin and the blood stream is slow and beaded However these changes are never so pro

(5) Brit. J Derm t. 70 37-43 February 1958

nounced as in true scleroderma with concomitant Raynaud's phenomenon and *most of the loops show none of the typical* dilatation of the central part nor indentation and aneurysms of the capillary walls and the distinct increase in size which are *typical of Raynaud's* disease

The authors conclude that so called acrosclerosis is in fact a typical diffuse scleroderma with prevalent changes in the upper extremities and face coinciding with Raynaud's phenomenon The term acroscleroderma is much better than *acrosclerosis* since it indicates a connection with scleroderma However it does not seem useful to restrict the term acroscleroderma to cases in which Raynaud's phenomenon precedes the development of scleroderma and in which the disease runs a slow course The distinction between acroscleroderma with and without concomitant Raynaud's phenomenon can be accepted in principle but there are no essential differences between the two varieties They run an identical course and Raynaud's phenomenon may appear at any stage or remain absent

► [The very distinct differences in the chronaxy values between diffuse and localized scleroderma on the one hand and long standing Raynaud's disease with sclerodermatous changes on the other and the differences in the capillaroscopic picture would seem to justify continued differentiation between these two conditions The fact that in some cases it is not possible clinically to differentiate clearly between them is not a convincing argument against this point of view The primary process appears to be in the blood vessels in Raynaud's disease with sclerodermatous change and in the connective tissue in scleroderma —Ed]

Cancer of Lung in Progressive Systemic Sclerosis R L Richards and J A Milne[6] (Univ of Glasgow) report 2 cases *in which cancer of the lung was associated with progressive* systemic sclerosis (generalized scleroderma) and review 4 similar cases from the literature Of the 6 patients 5 were women and were known to have had systemic sclerosis for many years before they died of carcinoma In at least 4 pulmonary manifestations had been present for a considerable time Therefore it is postulated that in these patients pulmonary fibrosis was a premalignant condition in which neoplastic changes eventually developed All 5 women showed diffuse interstitial changes of progressive systemic sclerosis in parts of the lungs unaffected by carcinoma but cystic changes were present in only 2 *All 5 had adenocarcinomas*

(6) Thorax 13 38 45 September 1958

or alveolar cell carcinomas, types which are thought to be unassociated with cigaret smoking or other irritant factors.

One of the patients with cancer of the lung and progressive systemic sclerosis had a clinical picture different from that of the others. The patient was a man who had a relatively short history. Until the terminal stages there was no evidence of pulmonary disease. At autopsy the parts of the lungs unaffected by tumor did not show either interstitial fibrous or cystic changes of progressive systemic sclerosis. In this case, therefore, the tumor and the cutaneous and vascular manifestations of progressive systemic sclerosis appear to have developed together in a patient with previously normal lungs. Further, this is the only case in which the tumor was a bronchial carcinoma of the small cell type which is believed to be associated with cigaret smoking.

Study of the literature revealed no good evidence of an intimate association between malignant disease in general and progressive systemic sclerosis such as is found in some cases of dermatomyositis. In most recorded cases in which neoplasia and systemic sclerosis coexisted the association appeared to be fortuitous. This makes it more likely that in the 5 patients in whom respiratory manifestations of systemic sclerosis preceded onset of malignant disease by several years there was some direct connection between the pulmonary changes of progressive systemic sclerosis and the development of lung cancer.

► [It is of course difficult to decide whether in these cases the malignant changes were an outgrowth of a premalignant sclerosis in the lungs or whether there was fortuitous occurrence of sclerosis and cancer in the same patient, or whether there was an association between malignant disease and scleroderma such as is found in dermatomyositis.

Lichen sclerosus et atrophicus is another sclerotic process in which malignant changes occur in exceptional cases involving the vulva. Here again one must ask: can lichen sclerosus et atrophicus be a premalignant condition or is the development of vulvar carcinoma in this condition fortuitous or perhaps precipitated by some third factor?—Ed.]

9. DISEASES OF THE HAIR

Is Alopecia Areata Psychosomatic? Psychiatric Study of 125 unselected patients is presented by Ida Macalpine[7] (St.

(7) Brit. J. Dermat. 70:121-131, April, 1958.

Bartholomew's Hosp London) Included were 14 patients with alopecia totalis and 11 with alopecia universalis Five patients were under age 10 52 were aged 10 29 and 68 were over 30 Fourteen had had other dermatologic conditions 6 had had other illnesses (gross obesity diverticulitis peptic ulcer pernicious anemia, tuberculosis and thyrotoxicosis) and 5 had had major operations In 3 patients, alopecia areata followed stitching of a scalp wound In 6 the condition followed childbirth and in 1, two attacks of alopecia occurred only during two pregnancies with subsequent recovery In 12, another member of the family had had alopecia areata

No psychiatric abnormality was found in 84 patients (67%) 27 patients (22%) were considered to have a mild psychiatric disturbance qualifying for the label 'neurosis and 14 (11%) had a severe psychiatric disturbance in the past or at present qualifying for the label psychosis' If psychologic factors play a significant etiologic role in alopecia areata the highest incidence of mental disturbance would be expected in the severest forms of alopecia if only because they usually result from repeated attacks However the largest percentage of patients with alopecia areata and totalis or universalis occurred in the psychiatrically normal group and the lowest percentage in the psychosis group A greater portion of patients with alopecia totalis or universalis were mildly disturbed than of those with alopecia areata To establish whether this is significant in showing that psychologic factors are important the author further compared the duration and number of attacks of alopecia with the degree of mental disturbance There was no significant correlation The somewhat higher incidence of mild mental disturbance in patients with the severer forms of alopecia may therefore be due to chance or to factors such as the increased liability to social embarrassment and isolation of severe alopecia Thus it may be regarded as more effect than cause

Only 1 of the 14 patients with severe psychiatric disturbance gave a clearcut history of alopecia developing at the time of mental breakdown with subsequent remission of both Six of the total group gave histories of mental or emotional trauma to which their alopecia had been attributed However careful investigation showed that episodes of stress by no means coincided with or were followed by at

tacks of alopecia Those which might have been pathogenic were not followed by attack and when alopecia was established it was not significantly influenced by amelioration or development of mental stress Where patients gave a history of mental stress preceding an attack of alopecia close scrutiny of their lives before and after revealed many other situations of equal or greater stress which had not been followed by alopecia

Psychotherapy was used in treating 35 patients who showed some degree of psychiatric disturbance Though many improved both in their attitudes to themselves and in their social relations in none was the alopecia influenced in any way Psychotherapy did prove helpful however in overcoming anxiety and depression caused by the baldness

The author concludes that the investigation produced no evidence for the widely held view that psychologic factors play a significant part in causing or precipitating alopecia areata The occurrence of alopecia areata in mental defectives also contradicts any significant etiologic role of psychologic factors or mental trauma

► [Macalpine's study strongly speaks against the suggestion or assumption frequently made in the dermatologic literature and textbooks that psychogenic factors are important in the etiology of alopecia areata and its more extensive variants As is probably well known by now the present editors of this YEAR BOOK and their immediate predecessor for many years have taken a critical attitude regarding the *indiscriminate* use of psychosomatic factors to account for various dermatoses of unknown or partially known causation —Eds]

Sudden Graying and Psychic Trauma in Alopecia Areata is discussed by G Klingmuller[8] (Univ of Bonn) It has been assumed that in aging the previously pigmented hair does not become secondarily apigmented but that it is replaced by gray hair Sudden graying of the hair was observed in the following patient

Man 6? felt slightly dizzy and excited as he had many times before Four days later he noticed on the right neck some loss of hair in a round area Within the next 3 days he lost over night on his pillow and in the morning while combing bunches of black hair Simultaneously he lost his dark eyebrows and beard hair Before his sudden hair loss his dark scalp hair was mixed with gray hair After 3 days when he had lost all his dark hair he started losing though much slower his gray hair

On hospitalization the general and neurologic examinations were negative The scalp hair was very thin sparse the hair evenly white

(8) Dermat 1 g 117 84-92 A gu t 19 8

The scalp was hypotonic felt fatty and when studied with a magnifying glass showed in many follicles black 1 2 cm long hair stump which could be easily expressed The fingernails were normal Subsequently the patient lost all his body hair Alopecia areata manifested itself during the follow up period Rich white hair appeared mainly in the occipital region in circular areas

Thus in the patient studied an acute alopecia areata caused the pigmented hair to fall out rapidly whereas the white hair remained longer giving the appearance of the hair becoming white rapidly No psychic trauma preceded the graying

► [A very reasonable explanation of the phenomenon of sudden graying of the hair Ephraim at the Skin and Cancer Unit observed a somewhat different sequence of events his patient first developed sudden graying of the hair and soon thereafter was found to have vitiligo! The occurrences described by Klingmuller and Ephraim may well furnish explanations for some of the other cases of sudden graying which have been reported from time to time —Eds]

Alopecia Perinaevica For 9 years M Quiroga and V Pecoraro[9] (Buenos Aires) observed 2 men and 1 woman aged 28 48 who had alopecia areata with a central pigment nevus (Fig 20) Each patient presented only 1 focus of alopecia suggesting that the inhibiting factor causing the hair loss has to be sought in the nevus The changes in the hair itself



Fig 20 —Papill matous pigment ne us in cent r of l pec a areat spot l m n 48 (Courtesy of Quiroga M and Pecoraro V Ha t t 9 377 378 Augu t 1958)

(9) Hautarzt 9 377 378 August 1958

indicated the same mechanism of hair loss as in the usual forms of alopecia areata

These findings could be compared with those in vitiligo permaevica or leukoderma acquisitum centrifugum In these diseases there are only achromic foci elicited by the pigment nevi Further the achromia itself does not differ from that in vitiligo proper

The alopecia permaevica may furnish further proof for the assumption that alopecia areata and vitiligo are both the results of a similar inhibiting neurotrophic activity This activity may occasionally emanate from a nevus itself

► [Another piece of evidence suggesting a close relation between alopecia areata and vitiligo However there are other possible mechanisms besides neurotrophic activity which could underlie both diseases —Eds]

Traction Alopecia The dermatologist has long been aware that persistent and prolonged traction of the hair may produce baldness Many recent writings devoted to care of the scalp and hair warn of the necessity of avoiding prolonged traction but despite these admonitions the pony tail hair style has remained popular

In the past a year Albert H Slepyan[1] (Univ of Illinois) observed 24 cases of alopecia of the scalp in young girls wearing the pony tail The earliest manifestation is a mild erythema about the follicles receiving the greatest amount of traction Occasionally some scaling is noted In some cases minute folliculopustules occur in the erythematous area After several months along the margin of the hairline or in the part of the hair occasional hairs appear missing giving the area a plucked look (Fig 21) In well established cases small oval or linear areas of baldness radiate in the direction of traction By the time alopecia is evident the scalp no longer appears reddened or scaly at the site In some cases the scalp hair appears thinned without evidence of gross baldness Since some patients wear bangs with the part 1 3 in behind the frontal hair margin inflammation or alopecia may occur at these sites Other areas of predilection are the midline of the scalp preauricular postauricular and nuchal zones

In all but 2 of the 24 cases the alopecia disappeared within 6 months after the hair style was changed and traction was relieved In these 2 the alopecia seemed less extensive

(1) A M A A h D 1 78 395 398 S p mbe 1958



Fig 21 —Marg n l n of em nt giving po t r cul a l n chal rea plu k d look (Courte y of Slepyan A H AMA A h De m t 8 39 398 S pt mbe 1958)

than when first seen but the remaining alopecia appeared complete

The term traction alopecia is suggested to describe those conditions which were hitherto de ignated as alopecia limi nari frontalis traumatic marginal alopecia and others in which persistent traction with it resultant inflammation and the sequelae of inflammation can be established

Unique Case of Trichorrhexis Nodosa (Bamboo Hairs) is presented by Earl W Netherton (Cleveland Clinic)

Girl 4 had dry ichthyotic kin and a generalized scaly dermatiti The eruption had been pre ent since birth and was compatible with a diagno is of erythroderma ichthyosiforme congenitum The hair on the scalp was dry fragile and lusterless Hairs on the occiput and sides of the scalp were no longer than 3-4 cm and fractured so ea ily that it was difficult to remove them from the follicle by traction

Microscopic examination of hairs from the scalp and eyel rows re vealed nodose swellings varying greatly in size The earliest indica tion of abnormality was a narrow indentation of the cortex of the hair forming a shallow sulcus which appeared to surround the shaft As the abnormality progres ed swellings of the shaft developed the sulcus enlarged and on the proximal portion of the hair shaft a concavity formed into which fitted the adjacent enlargement of the distal portion of the hair These combined changes resulted in formation of pseudo-jointed nodose swellings resembling the joints of a bamboo pole Cul tures of hairs showed no growth of fungi

Examination of the patient 7 years later revealed the same nodose wellings of the hair shafts The calp hair was till dry lusterless and abnormally short

This patient s fragilitas crinium and concomitant erup tion are considered to be essential components of a congeni tal ectodermal defect As in monilethrix the primary hair di turbance probably occurs within the hair papillae A bi op y specimen of the scalp was not obtained Several eminent dermatologists stated that they had not een similar nodo e wellings of the hair shaft

Nylon Brush Agnes Savill[3] report everal ca es of hair los resulting from use of hair bru hes with nylon bristles In most cases areas of alopecia appeared over the vertex Ex amination revealed short hairs with frayed end in the bald area In each ca e alopecia cleared rapidly when nylon bru hes were discarded and bristle brushes substituted

In recent years the old fashioned hair brush has become rare be au e it bri tle taken from hogs and wild boars of

( ) A M A A h D rma 78 483-487 O tobe 19
(3 B t J De t 0 96- 93 A g S pt 19 8

Siberia and the coldest regions of Manchuria are now difficult to obtain Nylon brushes have bristles composed of nylon monofilaments cut to the required length This process can leave an uneven square end which is injurious to the hair Some manufacturers have succeeded in producing a rounded end which is safe to use Other firms have replaced nylon with molded polyethylene quills which are smooth resilient and have rounded ends This insures that the hair shafts do not become entangled frayed or pulled out by the roots

► [In recent years we have seen an increasing number of young and middle aged women with diffuse alopecia of the scalp (see comment to article by Skog p 436) However nylon brushes did not seem to be the causal factor in our cases —Eds]

Keratodermatitis Follicularis Decalvans According to Frederick Reiss Milton Reisch (New York) and Constance Millett Buncke[4] (San Mateo Calif) mention is made of follicular hyperkeratoses associated with cicatricial alopecia in the European literature but few cases have been reported In the American literature except for Graham Little's disease (lichen planopilaris) consisting of the triad of lichen planus acuminate follicular lesions and alopecia no mention is made of a condition corresponding to that described in the following report

Woman 69 had pruritus and partial loss of scalp hair of 3 months duration Past history was negative except for diabetes Examination revealed partial but diffuse alopecia of the scalp and the outer third of the eyebrows Hyperkeratotic follicles were present in the area of alopecia and surrounding skin Hairs could be pulled out with ease leaving noticeable pits The plugs were in a patchy arrangement over the scalp and nape of the neck No excoriations were noted There were numerous discrete pinhead sized follicular hyperkeratotic slightly erythematous papules on the shoulders external aspects of the arms and lateral aspects of the face At no time during the period of observation was a lichen planus like eruption noted The oral mucosa was normal

The patient received vitamin A orally and 5% ammoniated mercury ointment locally A severe folliculitis developed This subsided but the hair continued to fall Alopecia of the scalp and eyebrows was complete 15 months after onset of the eruption

Microscopic examination of a lesion from the shoulder showed thinning of the epidermis in some areas There was a patulous pilosebaceous orifice filled with keratotic plugs In the corium just below this was an area of perivascular infiltration of lymphocytes histiocytes and chromatophores The sebaceous glands appeared normal

(4) A M A Arch Dermat 78 619-624 November 1958

Almost all the follicular ostia in a specimen from the scalp were filled with lamellated horny material Some of the follicular openings showed a cup shaped dilatation Several follicles were devoid of hair The outer root sheath was edematous Perifollicular infiltrate was sparse and composed mainly of lymphocytes and occasionally a histiocyte There was distinct evidence of scar tissue more pronounced around the hairless follicles

The authors feel that folliculitis decalvans alopecia cicatrisata lichen planopilaris lichen pinulosus lichen planus follicularis circumscriptus alopecia mucinosa and keratodermatitis follicularis contagiosa can be ruled out on clinical or histologic grounds Certain findings resemble those seen in lichen (keratosis) pilaris In extreme cases of the inflammatory type slight scarring may result but is rare However lichen pilaris has its onset in early infancy and comes to a standstill at maturity Furthermore complete baldness has never been observed in lichen pilaris

Ulerythema ophryogenes has certain features in common with the present case particularly the cicatricial atrophy affecting the eyebrows and at times involving small areas of the cheeks and scalp The present case also has some features in common with cases observed by Lang and by Strassberg and designated keratodermatitis follicularis atrophicans In these cases however the disease progressed rather slowly and did not produce complete baldness

Noncicatrizing Alopecias With Special Reference to Alopecia Areata William N New and Walter R Nickel[5] (US Naval Hosp San Diego Calif) point out that about 95% of all baldness is ordinary or common male baldness There are three main interrelated etiologic factors in this type of baldness heredity gonadal influence and age In sections of tissue from scalps with male baldness of long standing the sebaceous glands were numerous and large and the sweat glands appeared normal The number of hair follicles were reduced and the ones remaining were atrophic

Diffuse hair loss may result from medicaments (thallium and other heavy metal salts quinine Atabrine* Cyverine* barbiturates arsenic aminopterin reserpine coumarin heparin sulfonamides thyroid antagonists such as propylthiouracil and massive doses of vitamin A) or disease states (hypothyroidism iron deficiency anemia in women leukemia

(5) Calif Med 89 3 330 November 1958

diabetes, debilitation, impacted wisdom teeth, focal and general infections, acute systemic lupus erythematosus and fevers over 103 F.) Women may have diffuse hair loss post partum or after the menopause.

Alopecia areata is of special importance because 50% of the patients whose disease began before puberty eventually had alopecia totalis and 23% of those with postpuberal onset progressed to total baldness. About 75% of both groups remain totally bald. The cause and mechanism of production of alopecia areata is obscure, but the frequent association of psychic trauma is stressed by most authors. Treatment is of little avail. General use of corticosteroids is not recommended despite the improvement in scalp appearance observed in most patients in whom systemic administration of these hormones was used. Alopecia areata occasionally is simulated by other types of baldness, especially trichotillomania and alopecia resulting from use of hair waving solutions and hair straighteners.

In 22 patients with alopecia areata studied microscopically by the authors, the presence of huge patulous orifices devoid of hair and plugged with keratin detritus was a striking feature. Plugging was more pronounced than in lupus erythematosus. The epidermis was normal except for absence of pigment. In the dermis a constant inflammatory change occurred composed of lymphocytes related to the hair follicles and blood vessels, and in some instances to sebaceous and sweat glands. In all instances there was a relative or absolute absence of robust hairs in the areas of alopecia. Inconstant changes included fibrosis at varying levels in the cutis in relation to the follicles and an apparent superficial position of the sebaceous glands in instances in which there was no identifiable active formation of hair.

► [Macalpine (this YEAR BOOK, p. 261) was unable to substantiate the age old claim that there is a connection between emotional factors and alopecia areata.—Eds.]

Urticaria Pigmentosa Solitary Lesion Aaron Kaminsky Jorge Daitsch and Jorge Abulafia[6] (Buenos Aires) report solitary mastocytoma in 3 children (ages 1 year 2 years and 6 months) the first such cases in the Argentine literature One case is described

Boy 1 since birth had had on the upper thigh a single oval plaque 2×4 cm of reddish chamois color elevated not hairy with a slightly granulated surface Urtication occurred spontaneously and with scratching (Darier s sign) and spontaneous blisters appeared on several occasions The pruritus was worse at night and disturbed the child s rest History general and hematologic examinations and x rays of the skull and extremities were normal

Histologically this type of urticaria shows an intense infiltrate of variable distribution in the dermis consisting of mastocytes (demonstrated by metachromatic staining) In some cases these cells surround blood vessels and adnexa in loose clumps in others in a subepidermal layer and in some the mastocytic infiltration is extremely pronounced

Clinically the condition is characterized as follows It appears in the first months of life or is present at birth It has a nodule or plaque 2 3 cm in diameter which varies from reddish brown to yellow Urtication occurs spontaneously or with trauma often forming blisters or vesicles (an important diagnostic sign) Both sexes are equally affected The histologic picture is typical It behaves clinically like a nevus which it resembles In time the lesion flattens stops itching and forms blisters and in the course of years may disappear altogether No case has been described in which additional lesions have appeared or the process became generalized

Apparently there is little knowledge of this interesting form of urticaria pigmentosa especially among pediatricians Despite the paucity of reports it is probable that many cases remain undiagnosed and are confused with pigmented nevi So far no blood dyscrasias nor mastocytic foci in bones have been demonstrated in these cases of solitary mastocytoma No effective treatment has been found Antihistamines by mouth and parenterally and corticosteroids in ointments

(6) Arch g t d m t 7 47 257 Sept mbe 1957

and local injections relieve the pruritus but have no effect on the lesion

► [Solitary lesions of urticaria pigmentosa (mastocytoma or solitary mast cell nevus) have been described in increasing numbers (Chargin and Sachs A M A Arch Dermat & Syph 69 345 1954 and Drennan and Beare J Path & Bact 68 345 1954) It would seem that lesion which have a tendency to recurrent vesiculation might be subjected to various investigations including histochemical studies in the attempt to learn something of the mechanisms which lead to blistering —Ed]

Histamine and Related Compounds in Urticaria Pigmentosa *Analyses of Tissues Having Mast Cell Infiltration* Lytt I Gardner and Artelissa A Tice (State Univ of New York Syracuse) analyzed chemically tissue from the liver and spleen of a child with urticaria pigmentosa Both tissue were infiltrated with mast cells Trichloroacetic acid extracts of tissue from the liver were chromatographed on paper Histamine was found in the tissue in several hundred times normal concentration and exceeded the values for human tissue reported in the available literature Since the liver and spleen were extensively infiltrated with mast cells it seems likely that the excessive histamine was localized in these cells

No serotonin could be detected in these human mast cells in contrast with previous reports of increased serotonin content in rodent mast cells and in agreement with the findings of Sjoerdsma and associates who could find no serotonin in skin from a patient with urticaria pigmentosa The findings suggest that decarboxylation of 5 hydroxytryptophan to serotonin does not occur in the human mast cell Accumulation of compounds such as 5 hydroxytryptophan kynurenine or hydroxylated kynurenine may take place instead Measurement of activity of xanthine oxidase revealed no gross increase in activity in the mast cell liver Activities obtained were so low that nothing further could be concluded

Acetone extracts of tissue from the liver were made and the residues chromatographed Besides histamine three substances of unknown structure resembling tryptophan and/or its metabolites were noted Concentration of heparin like material in the liver was greatly elevated and the observed histamine presumably was the organic base in association with the organic acid heparin Whether histamine or heparin plays the primary pathogenetic role in urticaria

(7) Pediatrics 21 80 81 Ja 1958

pigmentosa is unknown Were either being overproduced or underconsumed due to metabolic error increased concentrations of the other compound in the tissues to satisfy the requirements of the law of electroneutrality must be predicted Since either histamine or heparin exert such potent physiologic effects in extremely small concentration in plasma there would be some survival value in maintaining excessive amounts of such compounds in an intracellular position

► [All presently available evidence indicates that the cutaneous mast cells in man contain histamine heparin and hyaluronidase but no serotonin. The question remains to be answered whether one or more of these substances or other as yet unrevealed substances in the mast cells produce the clinical manifestations of urticaria pigmentosa Baer Bersani and Pelzig recently observed 3 patients with urticaria pigmentosa in whom the oral administration of reserpine produced peculiar clinical manifestations These included a form of flushing in 1 patient and lessening of whealing in 2 others The possibility that these effects are the result of degranulation of the mast cell granules by reserpine has been considered.—F ls]

Spontaneous Histamine Shocks in Urticaria Pigmentosa

G Bloom H Duner B Pernow J Winberg and R Zetterstrom (Karolinska Inst Stockholm) report a case

Girl at birth had four red macules about 1 cm in diameter on the trunk The skin lesions increased in number and size and the color changed from blue red to brown Clinically and histologically the lesions were typical of urticaria pigmentosa At age 3 months she had a sudden generalized flush accompanied by extreme irritation then shortly became pale flaccid and unconscious At about the same time wheals appeared over the cutaneous lesions Some of the wheals were transformed into blisters Unconsciousness lasted several minutes This sequence of events occurred later on several occasions but unconsciousness occurred only twice At age 10 months two tumors about half the size of a hen s egg appeared on the skin (Fig 22) At this time pruritus was almost unbearable One tumor was removed surgically without clinical improvement Hydrocortisone 17 5 mg daily was injected into the second tumor for 9 days No macroscopic change occurred in the tumor and no clinical improvement followed

the lesion was excised surgically A few days later itching and attacks of restlessness disappeared Microscopic examination of the tumor revealed definite regressive changes in the mast cells resulting from local administration of hydrocortisone

Examination 6 months later revealed no recurrence of the cutaneous tumor The histamine content of two small skin lesions and urinary excretion of histamine were *markedly* elevated Urinary output of the hydroxytryptamine metabolite 5 hydroxyindoleacetic acid was normal

Urinary output of free histamine in the patient (and in 7

[9] Acta paediat. 47 152 16 March 1958

and local injections relieve the pruritus but have no effect on the lesion

► [Solitary lesions of urticaria pigmentosa (mastocytoma or solitary mast cell nevi) have been described in increasing numbers (Charem and Sach A M A Arch Dermat & Syph 69 345 1954 and Drennan and Peare J Path & Bact 68 345 1954) It would seem that lesions which have a tendency to recurrent vesiculation might be subjected to various investigations including histochemical studies in the attempt to learn something of the mechanisms which lead to blistering —Eds]

Histamine and Related Compounds in Urticaria Pigmentosa Analyses of Tissues Having Mast Cell Infiltration Lytt I Gardner and Artelissa A Tice[7] (State Univ of New York Syracuse) analyzed chemically tissue from the liver and spleen of a child with urticaria pigmentosa Both tissue were infiltrated with mast cells Trichloroacetic acid extracts of tissue from the liver were chromatographed on paper Histamine was found in the tissue in several hundred times normal concentration and exceeded the values for human tissue reported in the available literature Since the liver and spleen were extensively infiltrated with mast cell it seems likely that the excessive histamine was localized in these cells

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(7) Pediatrics 21 80 84 Ma 1958

liberation This fact might be explained by the finding that histamine in vitro blocks the anticoagulant effect of heparin in proportions larger than 20 1

► [Flushing and burning can also be produced by 5 hydroxytryptamine. However the fact that no 5 hydroxytryptamine has ever been found in the mast cells of man the absence of 5 hydroxyindole acetic acid in the pa tient s urine and the increa ed urinary excretion of histamine speak in favor of spontaneous hi tamine shock in this patient.—Eds]

Association of Functioning Carcinoid Syndrome and Scleroderma I Case Report is presented by Chris J D Zarafoneti Stanley H Lorber and Stephen M Hanson[9] (Temple Univ)

Woman 42 exhibited paroxysmal flushing of the skin associated with telangiectasia and *purplish red raised thickened areas on the cheeks and nose* (Fig 23) scleroderma like changes of the lower ex



Fig 23 —Purpl h ed sed d p lpal ly th ken d a o heeks a d nose (Court y f Zarafonet C J D *I I* A J M Sc 236 1 14 J ly 1958)

(9) Am. J M Sc 236 1 14 J ly 1958

others with urticaria pigmentosa) was abnormally high which shows that in this disease there is not only local histamine release on mechanical irritation but also constant flow of this substance into the circulating blood Thus on theoretical grounds the possibility exists that histamine



Fig. 22.—Note big elevated ulcerated lesion below left clavicle This is one of tumor like lesion which later was removed surgically (Courtesy of Bloom G et al Acta paediat 47 15 16 March 1958)

shock may appear if release of histamine into the blood is suddenly increased

Because the mast cells contain heparin and histamine it is surprising that there was no impairment of hemostasis in the present patient with massive *histamine release* whereas *in other patients* severe and even lethal hemorrhages have been reported with only minor symptoms of histamine

chronic endocarditis pulmonary and tricuspid valvular stenosis diarrhea and vasomotor disturbance She also had a pronounced cutaneous lesion indistinguishable from pellagrous dermatitis The extensor surfaces of the hands and forearms showed marked reddish brown pigmentation with hyperkeratosis and scaling From the knees to the ankle sharply demarcated above the skin was red brown glistening and tightly stretched over the underlying tissues which pitted on pressure The skin of the dorsum of the feet and toes was pigmented and scaly There was no abnormality of buccal mucosa however and no glossitis

Much of the dietary tryptophan in this disease is diverted from its normal metabolic pathway and is used as a precursor of serotonin thus inducing a relative deficiency of niacin Treatment with nicotinic acid in daily doses of 150 mg resulted in a decrease in the pigmentation and scaling of the skin but diarrhea increased in severity As surgical treatment of the primary growth was not considered feasible chlorpromazine an experimental serotonin antagonist was given in therapeutic dose but it did not alleviate symptoms The condition of the patient gradually deteriorated and she died about 3 years after onset of symptoms

Cardiac lesions skin and vasomotor changes asthma and diarrhea are now recognized as clinical features of the carcinoid syndrome and the level of 5 hydroxyindoleacetic acid in the urine is regularly increased in this disease This biochemical feature makes possible confirmation of a presumptive clinical diagnosis

The speed of growth and spread of carcinoid tumors vary but it has been shown that the primary tumor can produce a detectable increase in urinary 5 hydroxyindoleacetic acid before metastases occur Therefore an attempt at surgical resection is the first step in treating early cases Since the disease apparently progresses slowly even after metastases have occurred it may be of value to resect any large secondary deposits along with the primary growth to reduce the circulating blood level of 5 hydroxytryptamine Numerous experimental serotonin antimetabolites have been tried without significant clinical or biochemical improvement

Cutaneous Manifestations of Carcinoid Syndrome are described by Alvin S Zelickson (Univ of Minnesota) Carcinoid tumors are most common in the small intestine though all parts of the gastrointestinal tract below the esophagus including the gallbladder and appendix may be involved Reported extra alimentary sites include the ovaries and

(2 M w M d 1 N ml 1957

tremities colicky abdominal pain and diarrhea and cardiac murmur Attacks of flushing and edema could be precipitated by ingestion o small amounts of alcohol or by emotional stress Autopsy revealed ma lignant carcinoid of the ileum with metastases to the liver lung heart breast and appendix Fibrotic changes were observed in the liver inferior vena cava right heart skin of the legs and in associa tion with the tumor metastases

The fibrotic changes observed in the liver inferior vena cava and right heart are those classically associated with functioning carcinoid tumors Sclerosis of the valves of the right heart is believed to be due to an excessive amount of serotonin produced in the hepatic metastases and relea ed into the venous circulation Failure to induce similar altera tions in the left heart appears to be due to destruction of ser otonin by monoamine oxidase present in the lungs during the pulmonary phase of blood circulation

In view of the well documented propensity of metastasized functioning carcinoid tumors to produce fibrotic change in the right heart it is surprising that little attention has been given to the possibility that similar changes may be induced elsewhere in the body In the present case fibrotic change were found in the skin and metastatic tumor sites The pre ence of extensive scleroderma like changes in association with the other manifestations of fibrosis suggests the po si bility that all these findings might be directly due to the functioning carcinoid tumor The association of these finding has been interpreted by Zarafonetis as a possible clue to the pathogenesis not only of the fibrotic changes of the func tioning carcinoid syndrome but also of scleroderma and other fibrotic states It is theorized that such fibrotic change result from a deranged interaction of the serotonin mono amine oxidase mechanisms at the tissue level

► [The search for the cause of scleroderma and related diseases requires imagination and ingenuity Although the association of cleroderma and functioning carcinoid syndrome in this case may well be entirely fortuito it provides a lead which deserves further investigation MacDonald Rob bins and Malle y (Proc Soc Exper Biol & Med 97 334 1958) reported that dermal fibrosis can be deliberately produced by subcutaneous injec tions of serotonin creatinine sulfate in rats —I ds]

Carcinoid Syndrome with Pellagrous Dermatitis J M Bridges J B Gib on Lavinia W Loughridge and D A D Montgomery[1] (Belfast) report a case

Woman 60 had a malignant carcinoid with hepatic meta tase

(1) Brit J S r g 45 11 1 Septemb r 1 5

with interspersed blue areas In this stage the picture is one of a macular patchy purple cyanosis alternating with some areas of great pallor and others of brick red color nearly always confined to the face neck and extremities The flush may last 7 8 minutes and is usually accompanied by severe palpitation tachycardia bronchospasm and diarrhea Later in the disease course the cutaneous changes become irreversible constant and generalized The patient looks polycythemic and extremely plethoric because of permanent hyperemia of the face and neck with distended veins and profuse telangiectasia

A pellagrinous type of dermatosis has been noted in some patients with malignant argentaffinoma The lesions may look more pruriginous and less pigmented than those of true pellagra but diarrhea glossitis mental torpor and the typical pigmentation and scaling of exposed parts may be found It has been suggested that in the carcinoid syndrome all the available tryptophan is converted into 5 hydroxytryptamine and none is left for conversion into nicotinic acid Lack of the precursor of nicotinic acid thus leads to development of pellagra

Carcinoid metastases in the skin and subcutaneous tissues are rare Three cases were found in the literature and the author has seen another Palmar and plantar erythema in a patient with metastasizing argentaffinoma has been recorded and may be due to liver dysfunction The same patient also had neurodermatitis and vitiligo Another patient had acropachyderma

► [The average dermatologist is unlikely to be confronted with the full blown picture of metastasizing argentaffinoma because of the rareness of this syndrome Nevertheless it is of particular interest from the dermatologic viewpoint because of the pronounced cutaneous manifestations of flushing erythematous macular eruption of the extremities and pellagroid changes of the light exposed areas Whereas much knowledge has been gathered about 5 hydroxytryptamine (serotonin enteramine) and its occurrence in various species of animals and man much remains to be learned about the actual physiologic pathologic and clinical significance of this material in man —Eds]

Cutaneous Porphyria with Porphobilinogenuria Review and Report of Case Treated by Chelation are presented by Sherwin M Woods Henry A Peters and Sture A M Johnson[4] (Univ of Wisconsin) The patient represented an ex

(4) A M A Arch Derm 77 559 67 May 1958

lungs The tumors are composed of argentaffin cell which are normally found in these various organs The argentaffin cells secrete serotonin and glucagon Serotonin appear to play a definite role in the development of the syndrome Only about 20% of carcinoid tumors are malignant and the syndrome apparently occurs only in patients with metastases, especially to the liver

Abdominal symptoms are usually the first manifestation of the carcinoid syndrome Cutaneous symptoms soon become prominent Cardiac signs may not appear for many years The chief dermatologic manifestations are (1) reddish blue cyanosis of the face resulting from pulmonary stenosis (2) telangiectasia over the central portion of the face (3) thickening of the skin and urticaria of the face and (4) bright to deep purple flush brought on by alcohol emotion food spices or occurring with no apparent cause The flush begin abruptly with rapid spread from the neck to the chest and face including the conjunctivas and then to the upper arms There is increased warmth and a burning sensation in the parts affected with simultaneous bitemporal headache Symptoms subside after a period of 1 15 minutes leaving no residuals

Metastasizing Argentaffinoma from Dermatologist s Point of View According to Jean Walker[3] (Univ of Cape Town) cutaneous manifestations that have been seen in association with malignant argentaffinoma consist of vasomotor phenomena pellagrinou dermatoses palmar and plantar erythema neurodermatitis vitiligo and acropachyderma

The earliest and most obvious manifestation of the syndrome is a peculiar flushing which may be confused with the menopausal hot flushe of middle aged women The vascular symptoms may be transient or persistent but evanescent attacks of flushing are more characteristic A typical flush may be spontaneous or precipitated by alcohol chee e seasoned foods heat emotion standing or manipulation of the lower bowel by enemas It always starts with a subjective hot feeling and redness of the face quickly followed by the appearance of brick red spot on the limbs After 2 3 minutes the face becomes paler and the red spots may disappear or if the flush lasts longer they may become larger

(3) South African M J 31 12/1 1274 D 14 195

evaluation of this type of treatment in cases of porphyria

Clinical and Experimental Studies on Porphyrin Metabolism First Report R Schuppli (Univ of Basel) determined urinary porphyrin excretion routinely in many patients with various skin diseases No sex or age difference was found between patients with and without porphyrinuria Similarly extent of the skin lesion was not related to porphyrinuria Among various internal ailments only disturbed liver function seemed to influence porphyrin excretion Most patients who had abnormal liver function tests excreted large amounts of porphyrin Among skin diseases all patients with porphyria cutanea tarda excreted much porphyrin as well as coproporphyrin and uroporphyrin

An interesting finding was that among patients with contact eczema normal excretory values for porphyrins predominated and recurred almost with pathognomonic regularity Thus the author suggests that when eczematous patients excrete increased amounts of porphyrin some complication may be expected

About half the patients with actinic dermatoses showed normal porphyrin excretion When these patients were studied separately according to the type of dermatosis the eczematous forms were found to be accompanied by essentially normal porphyrin excretion whereas actinic dermatoses with urticaria were often combined with porphyrinuria Presence of the light band substance of Kimmig does not always imply light sensitivity Its excretion in various skin diseases did not parallel that of porphyrin

Porphyria was produced in rabbits with large amounts of allyl isopropyl acetyl carbamide (Sedormid[5]) but their skin did not show any change in reactivity when exposed to various physicochemical irritants

Porphyria Cutanea Tarda Tiong Hoo Tio (Surabaya Indonesia) and B Leijnse[6] (Rotterdam) describe a family in which 12 members in 4 generations were affected According to Waldenstrom's classification all the patients had porphyria cutanea tarda Application of the classification of Schmid Schwartz and Watson however causes some difficulties Neurologic and/or neurotic symptoms were found in 7 pa

(5) Dermatologica 116 289 299 Apr May 1958
(6) A M A Arch Dermat 77 568 575 May 1958

ample of hepatic porphyria cutanea tarda with evidence of latent and manifest porphyria in the maternal blood line First symptoms consisting of a vesiculobullous eruption on the exposed areas of the body after exposure to sunlight occurred when he was aged 16 He had mild hepatic impairment during attacks and spontaneously alluded to the correlation between his occasional use of alcohol and the onset of dark urine and skin lesions A liver biopsy specimen was histologically unremarkable

The patient was studied clinically biochemically and histologically for 2 years during which time the emergence of porphobilinogenuria was observed with manifestation suggesting that the syndrome might be merging into that seen in mixed porphyria in which abdominal or neurologic manifestations may coexist or alternate with cutaneous symptoms Significantly elevated excretion of porphobilinogen and its precursor δ aminolevulinic acid was noted during a cutaneous exacerbation and even higher excretion was present during asymptomatic remission Urinary excretion of these compounds in this patient not only suggested hepatic mixed porphyria but made likely the possibility of a future acute abdominal or neurologic episode and called attention to the absolute and mandatory avoidance of precipitating factors (alcohol sulfonamides barbiturate heavy metals etc) in management of such a case Failure to recognize this might result in the patient s death

Therapy with heavy metal chelates such as dimercaprol (BAL) and edathamil calcium sodium for acute intermittent hepatic porphyria has given highly favorable and often dramatic results in 14 of 21 cases seen by the authors When the patient was daily given 1 Gm edathamil calcium sodium orally he had no cutaneous exacerbations and said he felt more relaxed and mentally alert than ever before During the next summer he had no cutaneous lesions despite repeated exposure to sunlight incidental to his work He had no cramping constipation neurologic or psychiatric difficulty Urinary excretion of porphyrins and precursor did not seem to be altered however by edathamil calcium sodium therapy It is too early to speculate on the long term effectiveness of the chelation therapy but the patient s apparent favorable response is encouraging and suggest the need for further

evaluation of this type of treatment in cases of porphyria

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(5) Dermatologica 116:289-299, Apr.-May 1958.
(6) A.M.A. Arch. Dermat. 77:568-575, May 1958.

tients and slight lassitude in 5. Many patients had abdominal symptoms, and operations were performed in 7. Constipation was prominent in 5. These facts and the ages at onset (16-[illegible]) make it tempting to classify this family as having mixed porphyria, though an acute attack with positive porphobilinogen has never been observed. As the abdominal operations revealed abnormal conditions, as it is common to find persons with odd behavior among the general population and especially as one nonporphyric member of the family was mentally abnormal, the authors feel that this classification is not fully justified. Other writers have pointed out that no sharp distinction can be made among the several types of porphyria, and classification is sometimes only arbitrary.

The genealogic table of this family clearly shows a simple dominant inheritance. Slight liver impairment was present in some patients. All members of the family denied consumption of alcohol or barbiturates. All affected members showed hypersensitivity to sunlight. Photophobia was found in 2. No patient showed any particular ocular defect. In 2 the diagnosis of porphyria could be confirmed only by fecal examination. Three members of the family clinically became burned-out cases after about their 40th year.

Cutaneous Form of Hepatic Porphyria and Porphyrin Excretion in Urine were studied by G. Leonhardi and M. Maier[7] (Univ. of Frankfort). In disturbed porphyrin metabolism porphyrins accumulate which are intermediary products of hemin synthesis. Alterations in porphyrin metabolism can be recognized clinically and chemically. There is increased production of porphyrins that lead to changes in various organs causing symptoms in the skin, gastrointestinal tract and in the nervous system. There also are disturbances in porphyrin metabolism which do not cause clinical symptoms. In both instances the porphyrins are excreted by the kidneys and may be detected in the urine. It has been shown that in various forms of disturbed porphyrin metabolism there are certain differences in the urinary excretion of porphyrins.

The authors studied the urinary porphyrins and their isomers in 8 patients who had the cutaneous form of hepatic porphyria. The porphobilinogens, ether soluble porphyrins

(7) Arch klin u exper Dermat 07 554 575 1958

and ether insoluble uroporphyrins were determined quantitatively and the porphyrin components and their isomers were differentiated by paper chromatography In every patient urinary excretion of uroporphyrins was increased Some increase in urinary coproporphyrins and traces of proto and deuteroporphyrin in the urine was observed Two patients al o excreted porphobilinogen 1 of whom had symptoms of the combined form of hepatic porphyria in his clinical history

Uro and coproporphyrin isomers were estimated by intensity of their fluorescence by paper chromatography and were predominantly of type I

In cutaneous forms of hepatic porphyria the liver perform the decarboxylation and dehydration of uroporphyrin to protoporphyrin incompletely causing hemin synthesis in the liver to stop at the stage of uroporphyrins The manifestations of the disease may be due to disturbances in the enzyme systems of the liver

Hypertrichosis Melanosis and Circumscribed Dermatosclerosis Consequent to Subcutaneous Injection of Hematoporphyrin Followed by Solar Irradiation were seen by Xavier Vilanova and Joaquin Pinol[8] (Univ of Barcelona) in 2 patients These cases support the hypothesis that skin changes *in porphyria are the result of a local reaction to de*posits of porphyrin in the skin

A year before admission woman aged 40 received subcutaneous injections of hematoporphyrin solution in both arms as treatment for a psychic depression Two months after the last injection on the day following a sun bath circumscribed inflamed areas accompanied by swelling and severe pruritus and corresponding to the site of the previous injections were noted on both arms Symptoms gradually subsided leaving dark depressed and indurated plaques

Examination showed dark brown hard board like plaques slightly oval about 12 cm in diameter with a papular surface they were freely movable over the deeper planes The plaques also displayed striking hypertrichosis with long coarse black hairs limited strictly to the indurated pigmented surface Biopsy showed in the papillary body and corium bands of collagen compressed and lacking in fine structure with a sclerotic cicatricial appearance Between these bands numerous fibroblasts were dispersed without constituting foci of infiltration The elastic network had disappeared and capillaries were scant. The hypodermis was strikingly fibrosclerotic The interlobular septa were enlarged fibrosis penetrated the fat lobules which were reduced to a few

(8) Dermat logia Rev m x. 1 146-154 Oct D 1956

vesicles of fat surrounded by connective tissue fibers in some place and edema in others with the presence of lipophages In fibrotic areas principally in the cutis, fine dark red granules were scattered *diffusely* these were interpreted as the remains of injected porphyrin Pigmentation of the plaque was explained by an abundance of pigmented cells in the basal layer from which pigment extended toward the mucous layer across arborescent prolongations of melanocytes Dermal melanophages were absent The epidermis was perhaps slightly thinned and had an almost linear border due to sclerosis of the papillary layer The basal layer showed small areas of softening

► [In view of the fact that localized areas of scleroderma are sometimes seen in porphyria the report of sclerodermatous change produced by the local injection of a porphyrin solution into the skin is of special interest —Eds]

Tongue Pigmentation in Addison s Disease K Kitamura and Y Mishima[9] (Univ of Tokyo) report a case

Woman 44 for about 2 years observed a slowly developing brown discoloration of the skin all over the body Increased excretion of mineral corticosteroids in the urine was noted On physical examination the skin showed black brown pigmentation over the entire body Characteristically there was increased pigmentation on the extensor surface of the end phalanges as well as brown discoloration of the creases of the palms and soles which otherwise were not pigmented The lips were violet gray with many black dots The entire oral mucosa showed gray brown discoloration The whole tongue was covered with dark violet gray macules The bulbar conjunctiva bilaterally had rice kernel sized pigmented spots and the lid margins had similar pigmented dots

Biopsy of a skin specimen from the right leg revealed extensive melanin deposits in the basal layer of the epidermis down to the middle layers of the stratum spinosum Sparse chromatophores were noted in the upper layers of the corium The dopa reaction revealed quite a few melanocytes in the basal layer but the chromatophores in the corium were dopa negative Histologic examination of the tongue pigmentations showed no remarkable pigmentation in the epithelium whereas the papillary bodies of the mucosa below it were saturated with partly intracellular brown black pigmented granules Dopa staining revealed dopa positive melanocytes only in the epithelial cells close to the papillae whereas the pigmentation under the papillae in the stratum papillare was exclusively dopa negative

Dependence of the papillary pigmentation on the melanocyte accumulation above the papillae suggests that the melanocytes which are in a resting state in the basal layer of the suprapapillary epithelium are activated by corticosteroid produce melanin and discharge it as papillary pigmentation

► [While pigmentation of the buccal mucosa and gums is not uncommon in Addison s disease pigmentation of the tongue appears to be rare The authors state that administration of cortisone for 1 month caused lighten

(9) Hautarzt 8 484 486 November 195

ing of the skin color on the entire body but they do not report what happened to the pigmentation on the tongue —Eds]

Black Hair Tongue Comparative Study of Black Hair Tongue Geographic Tongue and Drug Eruption of Tongue based on clinical and histologic findings and a review of the literature is presented by Louis H Winer[1] (Univ of California Los Angeles) In black hair tongue (Fig 24) the flora of the mouth by increasing acidity inhibit the keratinase from desquamating stratum corneum The color is not



Fig 24 Black hair tongue (Courtesy of Winer L H A M A Arch Dermat 97 103 Jan 1958)

due to melanin but to keratin and the oxidation products of the oral flora Black hair tongue may be any color from yellow to black Yellow lesions contain less bacteria and more keratin whereas dark brown to black lesions contain not only increased keratin but also more candida organisms

Geographic tongue clinically because of its frequent recurrence configuration progress and histopathologic feature resembles a benign type of superficial pyoderma not unlike that of erythema streptogenes or so called pityriasis simplex Geographic tongue is an atrophy of the filiform papillae due most likely to excessive alkalinization and infection of the overlying epithelium The epidermal rete of geographic tongue is about the same thickness as that of black hair tongue if the stratum corneum is excluded

Orally administered antibiotics may produce epithelial hy

(1) A M A Arch Dermat 77 97 03 Jan 1958

Clinical Manifestations and Microscopic Findings of Black Hair Tongue Geographic Tongue and Drug Eruption

	Clinical Manifestations		
	Black Hair Tongue	Geographic Tongue	Drug Eruption
Location	Central posterior dorsum	Anterior lateral margins	No specific
Duration	Persistent	Evanescent	*Acute*
Symptoms	Nasty taste	Burning	Burning
Type of lesion Patches	Yellow brown black surface smooth to *rough*	Atrophic smooth red center gray elevated borders	*Smooth*
Border	Irregular	Arciform	Sharp annular
	Microscopic Findings		
	Black Hair Tongue	Geographic Tongue	Drug Eruption
Involvement Stratum corneum	Filiform papillae Increased and elongated cornified epidermal caps	Filiform papillae Denuded elevated with many P M N s	Entire surface Parakeratotic very thin
Epidermal red cells	Spindle shaped clear keratinizing cells intensely vacuolated	Slightly vacuolated round	No change in size thickened
Basal zone	Intensive increase in number of nuclei small round or cuboidal cells	Normal *nuclei columnar cells*	Normal nuclei, columnar cells
Cutis	No changes	epidermal cutis junction invaded by P M N s Inflammation in papillary bodies	Edema intimal *proliferation* many eosinophils and P M N s
Treatment	Vitamin A painting with 20% podophyllin in acetone alcoh l aa *trichloroacetic acid*	Dilute HCl antibiotic mouth wash	Interdict causative drug steroids

pertrophy of the filiform papillae Parenteral penicillin may produce proliferation of the capillary endothelium eosinophilic invasion in the perivascular areas of the papillary cutis and parakeratosis without hypertrophy of the stratum corneum The epidermal rete in drug eruption of the tongue is

twice the thickness of that seen in black hair tongue or geographic tongue The clinical and microscopic findings in black hair tongue geographic tongue and drug eruption are compared in the table

In 4 patients with black hair tongue painting with 20% podophyllin resin in equal parts of acetone and alcohol resulted in clearing in 2 weeks The patients were given vitamin A troches to prevent recurrence It is believed that after desquamation i accomplished vitamin A locally applied may interfere with sulfhydryl metabolism thereby inhibiting recurrence of the keratosis of black hair tongue Of 3 patients with geographic tongue 2 responded to 250 mg chlortetracycline dissolved in 120 cc water used as a mouth wash twice daily The third patient gave a history of indigestion due to achlorhydria By administration of 1 cc dilute hydrochloric acid 3 times a day both the indigestion and geographic tongue disappeared A patient with drug eruption of the tongue responded to steroid therapy in 1 week He was given 300 mg cortisone the 1st day 200 mg the 2d day and 100 mg daily thereafter

► [The author s clin cal description indicates that the term 'black hair tongue' alth ough generally accepted is a very inadequate name for these lingual changes The le ions are often neither hairy nor black. The finding that local Aureomycin® therapy is beneficial in some cases of geographic tongue s interesting There is no evidence that geographic tongue is due to nfectious micro organisms and ordinarily the involvement is of many y ars duration —Eds]

Linea Fusca (Brown Forehead Ring of Andersen Wernoe and Haxthausen) Thirteen Cases are reported by P J Michel (Lyons France)

The first cases of this peculiar brown arch on the forehead reported by the Danish authors cited were in patients with disea es of the central nervous system (particularly post encephalitic parkinsonism syphilis tumors syringomyelia etc) and were regarded along with other cutaneous changes (hypertrichosis eczema lichenified prurigo with pseudosegmental distribution) as an expression of central nervous system involvement especially of the mesencephalon The fir t case reported in France was by C Simon in 1945 Since 1949 about 20 cases have been observed in Lyons including the author s 13

Michel therefore believe that this pigmented line on the

I J A d mat yph 85 509 5 1 S pt Oct 19 8

forehead is not so rare as the Danish author thought The finding predominates in women and occurs under varied eti ologic conditions it is not always possible to determine whether or not these are coincidental Among condition noted in the patients studied were Parkin on s di ea e yphi



Fig 5—Lin a fu ca x t l w th ll f eckle (Co rt f M ch l P J Ann dermat et yph 85 509 5 I S pt O t 1958)

lis with and without involvement of the nervous system enteropathy pregnancy goiter and arthritis Five of the 10 women related the pigmentation to a previous pregnancy 3 said that the frontal line repre ented the remain of a chlo asma

These facts suggest that the anomalous pigmentation may have an endocrine sympathetic origin in an imbalance of hormones (hypophysoadrenal or sexual) and vitamins (C PP B_6) Regardless of whether or not thi hypothesis is cor

rect it seems certain that the original concepts a to cause pathogenesis and diagnostic value of the forehead line should be reconsidered in the light of the observations here presented

The typical line or band is about 1 cm wide with varying inten ity of pigmentation which is sometimes slightly lighter toward the center of the face and forms a loop de ign that may be more or less pronounced (Fig 25) Sometimes the pigmented line is prolonged toward the masseteric region but it is always parallel to the calp There i always a light trip between the hairline and the pigmented band

Melanoderma of Bright s Disease Two New Cases were ob erved by H Thiers Pierre P Ravault Daniel Colomb and Edouard Lejeune[3] (Lyons France)

Woman 60 was admitted for treatment of chronic azotemic nephritis At age 37 she had had acute nephritis with albuminuria and edema but without hypertension from which he had recovered in 2 months Four months before admi sion marke l asthenia developed accompanied by headache anorexia nau ea an l vomiting dyspnea on exertion and edema of the legs Her family physician then found nephritis with hypertension (240/130) and azotemia (0 90 Gm) De pite treatment the condition progres e l and examination on ad mis ion revealed severe clinical laboratory an l ocul r igns of chronic nephritis Blood urea ranged from 1 5 to 4 5 Gm

The patient exhibited a generalized pigmentation which was more prominent on expo ed part The face wa dull gray without pigmentation of the mucosa Forearms and leg were of a darker (dead leaf) lor limited to exposed part Nipple and genitalia were normally pigmented Al o pre ent s a diffu e cutaneou atrophy of the senile type

Skin biop y how ed marke l thinning of the epidermis which lacked papillae and con isted of only 3-4 cellular layers with disappearance of the granular layer The dermis was slightly atrophic but without infiltration or va cular lesions th only change was general *increase* of pigment in the basal layer of the epidermi Melanin stains confirmed the exi tence of an abnormal quantity of pigment which was seen in all layers of the epidermi including the corneal layers No pigment a found in the dermis

Skin finding in a woman 52 were imilar with melanin in all layers of the epidermi it was most marked in the basal layer Al o a moderate amount of pigment w is found in the dermis either free or within the cytoplasm of small histiocyte

The exact mechanism of melanoderma in Bright s disease

(3) A n. derma t yph 85 26 27 M y Ju 195

forehead is not so rare as the Danish authors thought. The finding predominates in women and occurs under varied etiologic conditions; it is not always possible to determine whether or not these are coincidental. Among conditions noted in the patients studied were Parkinson's disease, syphi-



Fig. 25.—Linea fusca associated with old freckles. (Courtesy of Michel, J. J.: Ann. dermat. et syph. 85:503, Sept.-Oct. 1958.)

lis with and without involvement of the nervous system, enteropathy, pregnancy, goiter and arthritis. Five of the 10 women related the pigmentation to a previous pregnancy; 3 said that the frontal line represented the remains of a chloasma.

These facts suggest that the anomalous pigmentation may have an endocrine sympathetic origin in an imbalance of hormones (hypophyseoadrenal or sexual) and vitamins (C, PP, B_6). Regardless of whether or not this hypothesis is cor-

Cutaneous Manifestations of Chediak Higashi Syndrome are specific and definite according to Dagoberto O Pierini and Jorge Abulafia (Bueno Aire) Only 3 cases of this hereditary malady have been reported previously The ash gray color of the hair the slate colored skin in exposed regions and the gigantic granules of melanin in histopathologic sections constitute a dermatologic triad which suggests the diagnosis This triad with granulation of leukocytes (neutrophil and monocyte especially) and ocular fundi characteristic of the albino are the most constant signs of the Chediak Higashi syndrome

Boy had ash gray hair at birth and at age 9 months slate gray spots appeared on the cheeks later similar patches developed on the forehead and extremities The skin remained smooth without notable change in thickness and elasticity Distribution of pigmented areas with sparing of the periorbital and peribuccal regions and a band about 5 mm wide below the hairline gave the face a peculiar mask like appearance

From the first months of life the child had repeated febrile illnesses secondary to sore throat or enterocolitis at times but often without evident cause At age 18 months a febrile attack associated with mucopurulent *rhinopharyngitis was accompanied* by adenopathy (retroauricular and inguinal) hepatosplenomegaly abdominal distention poor general condition pallor and marked photophobia Blood studies suggested the presence of leukemia and the patient was hospitalized for more detailed clinical study The ocular fundi were similar to those seen in albinos Hematologic study revealed marked anemia (7 45 Gm/100 ml hemoglobin) thrombopenia neutropenia (8-12%) and lymphocytosis (80 90%) Cytoplasmic granulations were demonstrated in the neutrophils of the peripheral blood and in the myeloid cells of the bone marrow The peroxidase reaction was at first negative but showed the characteristic staining later

Skin biopsy showed loose hyperkeratosis in the epidermis with large granules of melanin in clumps The granular layer was represented only by isolated cells The malpighian layer was of normal thickness with slight development of interpapillary crests Apical poles of basal cells and of some mucosal elements were occupied by accumulation of melanin granules of unequal size some extremely large The hypodermis was normal In some hair bulbs and in the cortical zone of hair roots gigantic granules of melanin were seen

After about 7 months the patient showed improvement on antibiotic treatment and repeated whole blood transfusions Later he had chickenpox and measles He was much improved at the end of 5 months During the next 3 years he continued to show susceptibility to infections

At age 4½ his general health deteriorated suddenly with reappearance of marked hepatosplenomegaly and recurrent febrile episodes

(5) Arch [illegible] gent derm [illegible] 8 23 31 March 19 8

is still to be elucidated According to Becher's theory the abnormal pigmentation is due to accumulation in the skin of aromatic substances of intestinal origin becoming brown under the influence of solar rays and retained in excess as a *result of the chronic nephritis* The xanthoprotein reaction of Becher and Jolles reaction measuring retention of indican were both strongly positive in these 2 patients These findings represent only part of the problem and much still remains unknown especially changes in activity of tyrosinase and in the cycle of the melano stimulating hormone

Skin Manifestations of Chronic Acidosis Edwin G Olmstead and John H Lunseth[4] (Marquette Univ) present 5 cases of dermatitis associated with chronic renal disease All 5 patients showed thickening of the skin drying scaling and loss of body hair particularly over the extremities The *most striking histologic finding* was an increase in elastic fibers in the papillary layer of the skin and in the perifollicular regions which seemed to be correlated with the degree and duration of the acidosis The fibrous tissue was not appreciably increased in any of these areas The degree of skin involvement clinically and pathologically was more closely related to the degree and duration of the acidosis than to any other single chemical abnormality of the serum Skin changes occurred in the presence of normal nonprotein nitrogen chloride and total serum osmolarity

The authors conclude that the elastosis in these patients resulted from conversion of nonelastin (for the most part collagen) to elastin in the papillary and perifollicular regions the conversion being in some way due to acidosis In favor of such a conversion is the close chemical similarity between collagen and elastin and the fact that collagen has been converted into elastin in vitro by treatment with 1% sodium m periodate at pH 5 and with dilute acid or alkali

Clinical improvement of the skin lesions with loss of itching and regrowth of hair occurred in 2 patients with chronic acidosis treated with sodium bicarbonate for 8 and 5 months In 1 case repeat biopsy after treatment showed normal histology

Skin changes similar to those seen in patients with chronic acidosis did not occur in a patient with hyperchloremia hypernatremia and hyperosmolarity of 7 years duration

(4) A.M.A. Arch Dermat 77 304-313 March 1958

Canizares Fabio Uribe Jaramillo and Franci co Kerdel Vegas[7] The reaction was observed frequently in the e coun trie where a commercial preparation containing monoben zyl ether of hydroquinone may be obtained over the counter with out pre cription Mo t cases occurred in patients with a highly pigmented kin Some were pos ibly Caucasian bru nette but mo t pre ented evidence of mixtures of Cauca ian Indian and/or Negro blood

In all ca es the equence of events wa a follow The pa tient applied a preparation containing monobenzyl ether of hydroquinone to the face for 2 weeks to a few months An acute contact dermatiti developed on the affected areas It u ually ubsided if treatment was di continued and oothing medication applied In rare ca e there was no hi tory of dermatitis though some patients had pruritus which may have indicated a ubclinical dermatiti Two weeks to 2 months after di appearance of the contact dermatiti area of depigmentation mixed with area of hyperpigmentation developed on the area previously affected and on their pe riphery Lesion at a di tance uch a on arm abdomen and legs were al pre ent in some patient In mo t ca e no explanation could be offered for the location of the di tant le ion The dy chromia alway consisted of round or oval macule and no in tance of linear or angular hape wa ob erved

Evolution f the le ions wa characteristic They pread and extended for 1 2 months and then were stationary Some times there wa spontaneous regression If the le ions were treated with methoxalen hyperpigmentation appeared more consistently in the acquired leukoderma than when rigmal patche of vitilig were treated with the ame med cation Severer reaction to this medication were found in thi type of leukomelanoderma than in true vitiligo

Mo t patient had applied a 20% concentration of mono benzyl ether of hydroquinone obtained in a commercial prep aration Some patient treated by dermatologists had used preparation containing 2 10 in an ointment ba e or in alcoholic tincture

The author conclude that treatment of le ion such a chl a ma in patient with a naturally hyperpigmented skin with preparations containing monobenzyl ether of hydro

(7) AMA Arch D mat 77 70 3 February 1958

Three months later, jaundice developed and he was rehospitalized There was marked anemia (8 77 Gm /100 ml hemoglobin) leukopenia (3 000 white cells) neutropenia (12%) and lymphocytosis (80%) Five months later the general downhill course was aggravated by pleurisy A month later generalized convulsions were followed by amaurosis which was controlled after administration of chlorpromazine for a few days The general state deteriorated slowly and abdominal distention increased Neurologic signs included headache transitory parese tremors and emotional instability The EEG revealed marked paroxysmal dysrhythmia with disorganization of bioelectric activity but no focal signs The patient died about a month after his 5th birthday There was no autopsy

Incontinentia Pigmenti Report of a Family Incontinentia pigmenti usually begins in early childhood a series of linear and grouped vesicles on an erythematous base which when ruptured tend to become impetiginized These may disappear and recur for weeks or month gradually giving way to an intermediate temporary stage of linear verrucous lesions or the vesicles may lead directly to the third or pigment stage characterized by a reticulated pattern of pigmented macules whorls lines and patches Many years later in some patients a final stage may occur in which the lesion fade leaving no blemishes or slightly atrophic slightly depigmented areas to mark the sites Many cases are associated with mild to severe ecto and mesodermal defects

Sophocles D Marty H Bernard Bechtel and Clayton I Wood[8] (Indianapolis Gen l Hosp) report a family tree in which all the female members (5) for three generation showed the cutaneous lesions of incontinentia pigmenti These patients tend to upport the sex limited mode of inheritance One male member of the second generation had developmental defects without skin lesions Because no defects were found in any other members it remains conjecture whether these defects were associated with incontinentia pigmenti or were mere coincidence The fourth stage is often overlooked Two of the present patient are in this stage 2 others passed through this stage and their condition stabilized with minimal pigmentation The fourth stage make acquisition of detailed family histories difficult because patients tend to forget skin blemishes of their childhood

Leukomelanoderma Subsequent to Application of Monobenzyl Ether of Hydroquinone Vitiligoid Reaction Observed in Colombia and Venezuela is described by Orlando

[8] A M A Arch Dermat 8 60, 611 November 1958

tion (seropapule) If such an early lesion is scratched off the epidermis is usually missing in the central areas

Chronic papular urticaria has to be differentiated from lichen prurigo and urticaria

Treatment depends on the patient age Women in the climacteric or menopause may be treated with corpus luteum During pregnancy local treatment is sufficient since the disease usually subsides after pregnancy Local therapy consists mainly of antihistamines Occasionally good results were seen after infiltration of the subcutaneous tissues of the affected area with Sympocaine* which is a procaine derivative with depot effect Under this treatment even distant lesions seemed to disappear

► [Much remains to be learned about chronic papular urticaria acne urticata and other pruritic papulourticarial eruptions of the face upper chest and back which have been described under various names Some seem to be acneform eruptions in individuals highly susceptible to itching who scratch and pick the lesions Others are associated with polycythemia leukemia drug and light sensitivity and hormonal disturbances or are lesions locally produced by cosmetics —Eds]

Further Observations on So called Lichen Vidal Urticatus A Greither and H Tritsch[9] (Univ of Heidelberg) studied 17 women and 7 men with lichen Vidal urticatus The women were pregnant climacteric preclimacteric or showed other disturbances of sex hormones Localization of the skin lesion varied in some patients the trunk and limbs were simultaneously affected in others the trunk was not affected (Fig 26) whereas in another group the papules showed distribution similar to acne vulgaris Notwithstanding the differences in localization the clinical appearance was rather similar in all the patients scratched flat nodules usually covered with crust were spread widely and there were many pigmented scars of similar size Severe itching was not diffuse but was limited to the papules subsiding as soon as the lesions were destroyed by scratching In several patients lichen Vidal urticatus and lichen chronicus Vidal were present together

Development of lichen Vidal urticatus begins with edema in the upper corium accompanied by acanthotic widening of the epidermis The edematous swelling of the connective tissue combined with further acanthotic widening and hyperkeratosis of the upper corium will lead to the fully developed mixed papules of lichen chronicus Vidal All other

(9) H[illegible] 9 198-203 May 1958

quinone is hazardous The leukomelanoderma which de velops in many cases is cosmetically more objectionable than the original hyperpigmentation

► [Monobenzyl ether of hydroquinone may produce excessive depigmenta tion especially in colored persons even when used under careful medical supervision However apparently it does not produce these leukomelano dermic changes in the e patients except after engendering a contact (aller gic) dermatitis —Eds]

Urticaria Papulosa Chronica From their studies on 11 women and 1 man aged 23 53, O Braun Falco and U M v Lückstedt[8] (Johannes Gutenberg Univ) learned that this condition is a well defined clinical entity It usually starts with small nodules on a healthy skin The intense itching accompanying the nodules subsides as soon as the lesions are scratched off The typical skin changes consist of eroded blood crust covered pinhead to lentil sized eruptions and of hyperpigmented or pale atrophic areas of former healed eruptions The lesions do not form groups or coalesce Sec ondary infections are rare Involvement of the oral mucosa was not observed

The disease affect mostly women Of the 11 women all but 2 had sex hormone disturbances The skin change sub sided after hormonal treatment or delivery The only man in the study group had had one of his testes removed before the skin erupted the other testis was atrophic The e observa tions support the assumption that chronic papular urticaria is due to hormonal dysfunction However it was not possible to identify the actual dysfunction responsible for the disease

The histologic picture depends on the stage of the disease In fresh lesion the epidermis is somewhat widened Often there is some tendency to proliferative hyperkeratosis lead ing to widening of the stratum granulosum Inter and intra cellular edema (vacuolation) is visible in the deeper layer of the stratum spinosum The dermal changes affect mostly the papillary bodie and superficial part of the reticulum layer The edematous connective tissues contain particular ly widened vessels surrounded by loose lymphocytic and eosinophilic infiltrations The perivascular infiltration ex tends into the area of the sweat gland The latter are not affected In the disease course cavitie filled with blood se rum leukocyte and possibly erythrocytes develop in the upper parts of the epidermis leading to typical vesicle forma

(8) Hautar t 8 534 40 December 19

Basic changes in acne urticata con i t of inten ive red millet sized urticarial papules or nodule that are crowned by a hardly visible bli ter and may be urrounded by an in flammatory halo Inten ive itching i characteri tic and i es entially limited to the primary lesions and their vicinity Hi tologically the acne urticata le ion are characterized in the beginning by edema of the cutis later al o of the epider mi with sub and intraepidermal vesicle formation and by

Acn cc d j fill (B ocq) B l m m d or f l l b os th l ll l d t f t l f nt l H pe p gmentat on m m l (C rt y f S lt ld K H t t 8 46-549 D embe 1957)

necro is of the epidermis and papillary bodie without pri mary involvement of the follicle Acne like change are ab *ent*

Neurotic excoriation lead to excoriation in the face like the above two entitie but may al o be found in any other areas within reach of the scratching hand There are no ba ic pathologic change The cause for scratching lies in the p ychic abnormality (hysteria) of the patient

The author believes that there is clo e relation between a ne urticata and urticaria papulo a chronica Acne urticata and acne excoriee hould be differentiated from acne necrot ica Boeck The papulonecrotic lesions good therapeutic re pon e to leukomycin and re idual varioliform car are typical of acne necrotica

In treatment of acne urticata if correction of basic medical (hormonal) or gynecologic abnormalitie fails edation and

features such as the subcorneal vesicles necrotic changes of the epidermis crust formation and hemorrhages are secondary and due to scratching

In differential diagnosis lichen urticaria and prurigo must be considered The common feature with lichen is the similarity of the papules However lichen Vidal urticatus does not cause lichenification of the skin Clinically lichen Vidal urticatus has not much in common with urticaria Histo

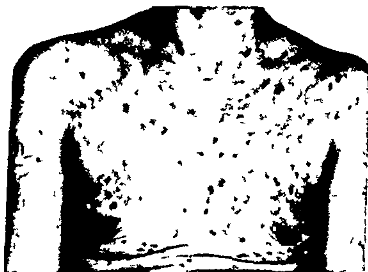


Fig 26 — Tru k mor invol d th n lin! (Co tes of Grether V a d Trisch H Hautarzt 9 195 03 May 1958)

logically edema is prominent in the connective tissue which in urticaria is not accompanied by acanthotic widening of the epithelium In prurigo nodularis and lichen Vidal urticatus itching is in the foreground but in the latter the individual lesions seem smaller than in prurigo nodulari

Differentiation between Acne Urticata (Kaposi) Acne Excoriee des Jeunes Filles (Brocq) and Neurotic Excoriations is analyzed by K Salfed[1] (Johannes Gutenberg Univ) Acne excoriee and acne urticata are two well defined completely separate *entities that have only their names in* common In acne excoriee (Fig 27) which is limited to the face and affects almost exclusively females aged 16 24 the patient is stimulated by the basic changes of acne papules and comedos to scratch the face Itching is not more pronounced than in acne vulgari

(1) H ut t 8 46 549 December 195

Basic change in acne urticata con i t of inten ive red millet sized urticarial papules or nodules that are crowned by a hardly visible bli ter and may be surrounded by an in flammatory halo Inten ive itching i characteri tic and i es entially limited to the primary le ion and their vicinity Hi tologically the acne urticata lesion are characterized in tl e b ginning by edema of the cuti later al o of the epider mi with sub and intraepidermal ve icle formation and by



F g — Acn e ri d) fill (B ocq) B d m y c m l on f l d bov os th se l w ll al ed t on lat l f on l e ll perp mentation m mal (Court y f S lf ld K H t 8 546-549 De mbe 19)

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In treatment of acne urticata if correction of basic medical (hormonal) or gynecologic abnormalitie fail edation and

antiurticarial care are in the foreground. Treatment of acne excoriée is the same as in acne vulgaris.

► [To the uninitiated and those not specially trained in dermatology the differential diagnosis of the various acneform eruptions of the face may present many difficulties. It is only through accurate diagnosis that appropriate therapy can be planned.—Eds.]

Acne Urticata Polycythemica: Report of Case is presented by Donald L. Baxter and James H. Lockwood (U.S. Naval Hosp., Philadelphia). This is the 15th case reported in the literature and the 4th in which oxidase granules were demonstrated in the cellular infiltrate.

White man, 66, had a skin eruption for about 3 months. The eruption was generalized, sparing only the face, palms and soles and partially sparing the middorsal back. The lesions consisted of erythematous macules, papules, excoriations, hemorrhagic crusted papules, pure vesicles and bullae on normal appearing skin and pustule-surmounting papules. There was superficial scarring at the site of former lesions. On both feet there were scattered bullae and bloody ulceration at the sites of former bullae. An ulcer on the dorsum of the left great toe was secondarily infected.

The patient's complexion was ruddy, with injection of the conjunctivas and mucous membranes. The lower extremities were of a dusky violaceous hue, with marked superficial venous congestion when dependent. Repeated determinations revealed the hemoglobin to be 19-24.4 Gm., red blood cell count 6,060,000-7,660,000 and hematocrit 62-70 vol. %. The white blood cell count was 12,100-22,250, with 75% segmented neutrophils, 1% band cells, 19% lymphocytes and 5% eosinophils. Blood volume studies with Cr^{51} showed a total volume of 8,820 cc.; the red cell volume was 6,086 cc. Sternal puncture revealed hyperplasia of all the cellular marrow elements. Chest x-rays revealed prominence of the perivascular markings and hilar vasculature, with borderline enlargement of the cardiac silhouette and left ventricular prominence consistent with the clinical findings of polycythemia.

After 2½ months' observation and study, the eruption subsided without treatment. Treatment of the polycythemia was then started. The patient was bled a total of 3,255 cc. in about 500 cc. increments during 3 weeks. Though there was marked improvement in the ruddy violaceous hue of the skin, new erythematous urticate papules started to appear after 2,230 cc. blood had been removed. The recurrent eruption subsided during the next 2 weeks, with continued phlebotomy.

Histologic examination of an urticate papule revealed a cellular infiltrate of eosinophils, polymorphonuclear leukocytes and mononuclear cells throughout the upper dermis and papillae, and a light infiltrate deep in the corium. After a saturated solution of benzidine dihydrochloride in 0.2% hydrogen peroxide and 40% ethyl alcohol was injected into a papule according to the technic of Weidman and Klauder, peroxidase granules were demonstrated in the macrophages, scattered throughout the dermis and in the eosinophils, which were so heavily

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( ) A.M.A. Arch. Dermat. 78:353, Sept., 1958.

hiden as to be ob cured by brown pigment in vitally stained pecimen whereas they were numerou in other biop y specimens

Further study i nece sary to ascertain whether the peroxi da e reaction i a con tant finding in acne urticata poly cythemica and to determine the significance of the peroxi da e po itive macrophages found in the cellular infiltrate

► [The clinical manifestations of polycythemia are many and varied. The possibility of its occurrence should be considered in patients particu larly in men who have a florid flushed appearance or in tho e who present b za re urticarial lesion —Eds]

Eczematid like Purpura M Binazzi and A I Lunzi[3] (Univ of Perugia) report 2 cases

CASE 1 —Man 45 in good general condition had noted 6 years be fore a brownish red lesion painless and nonpruriginous about 5 cm in diameter on the inner malleolu of the left leg This remained un changed until 10 months before ob ervation when a punctiform pur puric le ion appeared at the edges of the initial lesion which at this time regre sed Similar lesion appeared on the same leg the other leg the thighs and within 40 days on the trunk mainly the wai t and glute al region Itching inten e at the outset and during the period of di semination decreased a the le ions tended to form irregular group in reticular di tribution with superficial lichenification and caling in which the purpuric feature tended to les en Purpuric lesions were noted in the oral mucosa and there were focal infections of the tonsil and teeth The tourniquet and capillary fragility te ts gave no signifi cant re ults laboratory findings were negative and the histologic find ing conformed to those de cribed by Doucas and Kapetanakis Quick but tran itory benefit were derived from predni olone therapy but wide spectrum antibiotic were ineffective

CASE — Man 68 father of patient in Case 1 with whom he lived w in t ir health although he had had a history of chronic gastritis r ce t g 40 and of nervou breakdown Red itchy at times exu hit e le ion had appeared in the presacral region and inner malleo lu of the right leg 3 year before and had receded spontaneously 4 months before ob ervation Two months later small puncta and red p t developed on the legs and gradually on the thighs abdomen houlders and forearm always accompanied by pruritus which wa e pecially inten se at night The course of the dermatitis and the clini al laborat ry and hi tologic findings as well as the therapy and it re ult were imilar t those in Case 1

The literature ugge t that eczematid like purpura i an acute epidermiti probably secondary to a proce s of acute recurring capillaritis The authors advance the hypothesis that the condition probably ha infectious etiology and path genesis of microbic type in which both capillaries and epithelial tissue may be attacked The results of predni olone and antibiotic therapy seem to support thi hypothe is A

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virus etiology is excluded in view of the good general condition of both patients, the normal protein picture, and the absence of hepatic and medullary alteration. The possibility of its being a genodermatosis is also excluded.

Schonlein-Type Exanthema with Peculiar Disturbance of Blood Clot Retraction was observed by G. W. Korting, H. K. Peller and G. Koppel[4] (Univ. of Tubingen) in the following case.

Man, 48, had diarrhea followed a few weeks later by a rash covering the whole body. Two weeks later slight fever and moderate joint

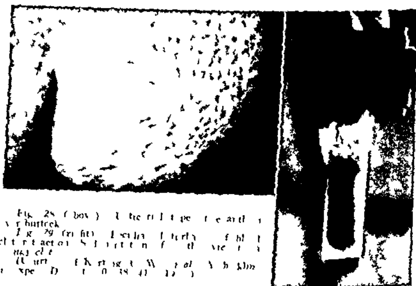


Fig. 28 (above). [illegible] on buttock.
Fig. 29 (right). [illegible] clot retraction [illegible]
(Courtesy of Korting, G. W., et al.: [illegible] 38, 41 [illegible])

symptoms developed. Physical examination revealed a somewhat enlarged liver. The skin exanthem affected practically the entire body except the face, neck, anterior and posterior surfaces of the chest and upper part of the scrotum. The buttocks were prominently involved. The skin changes were composed partly of pinpoint sized hemorrhages similar to those seen in scurvy or in Werlhof's disease and partly of lentil sized light red areas of erythema. Some were slightly elevated [illegible] (Fig. 28) and showed, after the edema had disappeared, pinpoint sized hemorrhages within the erythema as seen in nonthrombopenic (Schonlein) purpura. There were no hematomas. Pinpoint sized hemorrhages were also observed in the [illegible] on the lips and back of the tongue. During the 3d hospital week hematuria appeared and the blood pressure, which was normal before, rose to 180/120 mm. Hg.

The skin biopsy specimen showed the typical picture of Schonlein purpura. The most striking laboratory finding was the disturbance in com

(4) Arch. klin. u. exper. Derm. [illegible]

blood clot retraction (Fig 29) The routine coagulation te t (hep irin tolerance Quick s test recalcification time) showed normal v dues There was a compensated serum di turbance due to in ignifi cantly diminished factor IX Electron micro copic studie lid not how any morphologic changes in the thrombocyte of the patient H wever there was a tendency to increa ed adhe ion and concentra tion of thrombocytes into giant clumps which might have hindered the level pment of an organized fibrin structure leading to disturbed clot retraction as is true when agglutination is absent

In thi patient there was probably some etiologic relation between the skin exanthem and disturbance in the clot re traction mechanism

Hyperergic Panvasculitis with Multiple Symmetrical Skin and Bone Gangrene is discussed by A Matras[5] (City Hosp Vienna Lainz) The skin lesions in angiitis vary As

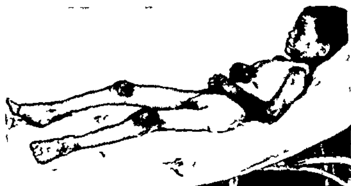


Fig 30 Symmetri lly loc l d p fic l k ee bo t 4 week ft se f d se se (C rt y f M tra \ \ h kl pe De m t 207 5 1 540 1958)

in periarteriti nodosa there is multiple circumscribed nod ular thickening of muscular type in the small and medium ized arterie of one or several organ systems includin, the kin The kin manife tations of periarteritis nodo a may be n dular purpura like or gangrenous The diagno i is facili tated by nodular den ities in the subcuti I anva culiti led t kin and bone gangrene in the case de cribed

I I ving mea le at age 5 had attack of swollen joints fever n l rythem multiforme like skin eruptions whenever some purulent t th r t were extracted The ruptions finally develope l into exten e over tic gan renou skin changes They were symmetrically lo calized over exten ive areas of the upper and lower extremiti s (Fig 30) an l over the buttock an l sacral region Be i l s there

5) Arch I pe De m 07 5 1 540 19

were circumscribed necrotic areas on the lips tips of the nose and tongue, buccal mucosa and ears

Treatment with antibiotics sulfonamides, ACTH and cortisone resulted in temporary improvement to the patient Following complete mummification of the necrotic skin areas the end and middle phalanges of all fingers fell off These phalanges and the urine contained much porphyrin Severe peritonitis due to perforating ulcerations of the stomach and bowels led to death 2½ years after onset of the disease

Histologically there were severe vascular changes in the skin and bowel walls consisting of fibrinoid necrosis of the media and leukocytic infiltration in the vascular wall and occasionally also thrombus formation

It is believed the patient had the cutaneous gangrenous form of hyperergic panvasculitis due to an infectious toxic process

Trisymptomatic Syndrome of Gougerot (Dermal Nodular Allergids) Is It a Lesser Form of Periarteritis Nodosa? This question is discussed by P Temime and A Rodde[6] (La Timone Hosp Marseille France) based on the following case

Man 47 had a history of alcoholism malaria and serum sickness after diphtheria His present illness began in August 1956 with a poor general condition fever and malaise followed by eruption of cutaneous nodules on the legs and arthralgia with swelling of the finger wrists knees and ankle which responded to treatment with Alcacyl Later there was parallel progression of cutaneous and joint manifestations of longer duration which required hospitalization in October 1956 and corticotherapy In May 1957 there were polymorphous cutaneous eruptions on the arms and legs consisting of papules purpuric nodules and pustules pruritus and enlarged lymph nodes The temperature subsided under Butazolidin* treatment and the joint pain lessened somewhat In September 1957 examination showed urticarial plaques dermal nodules pigmented macules (scars of previous nodules) significant adenopathy in inguinal axillary and epitrochlear glands Antiallergic and antihistaminic treatment was continued but the urticarial plaques and skin nodules persisted Some were purpuric and painful Antiallergic treatment with vitamins for capillary protection and then delta hydrocortisone in large doses were given Since November 1957 the cutaneous and joint symptoms regressed strikingly but manifestation of arteritis increased with necrotic ulcers of the 2d and 3d toes and absence of pulsations in the leg

The authors believe that the lesions in this case were not merely coincidental and that Gougerot's syndrome is a minor form of periarteritis nodosa further that other syndromes, including anaphylactoid purpura vasculitis of hypersensitivity granulomatous vascular allergid Horton

(6) Rev l on med 4 9 434 March 1958

syndrome nodular vasculitis and Still's disease may be related. In all these conditions there are vascular changes and inflammatory infiltrates in the skin and also in the viscera and lymph nodes. In all the etiologic factor appears to be allergic with resulting arteriolitis or necrotic arteritis and they often respond to the same treatment, i.e. corticotherapy. Whether the changes produced are cutaneous or visceral or both depend on the intensity of the etiologic process, predisposition—acquired or spontaneous—and localization (capillaries, arterioles, arteries of small or average caliber). Anatomico-clinical manifestations may be of various types: benign, acute with a single attack, as in anaphylactoid purpura; chronic recurring, as in dermal nodular allergids; severe (allergic granulomatosis) or lethal, as in periarteritis nodosa of slow or rapid progression. Polymorphism and differing courses of these various affections derive from the localization and variable intensity of the pathologic process.

Hypodermic Vascular Allergids. P. Duperrat and J. Monfort (Paris) examined the evidence for and against the allergic origin of various lesions including Gougerot's nodular allergids, periarteritis nodosa, nodular vasculitis, Bazin's erythema induratum, erythema nodosum, migrant thrombophlebitis and panniculitis (Weber-Christian disease). Based on a review of Montgomery's description of nodular vasculitis, 25 cases of this type were studied. All patients were women aged 23-68 (average 43). Only 2 had a history of asthma or eczema. The illness began with heaviness in the legs and unexplained asthenia, sometimes swelling of the ankles, followed by sudden appearance of nodules, often within 24 hours. Only 2 patients had varices. The course was subacute, often lasting for years, and each attack (often seasonal in March to April) was preceded by asthenia and leg pains.

Investigation of the focal sepsis revealed 5 patients with a history of pulmonary tuberculosis, 2 rheumatic carditis, 8 furuncle, 7 genital suppuration, 5 infections of digestive tract and appendicitis, 2 repeated anginas and 4 dental complication. Some patients had had several infections. In 5 there was no history of focal sepsis. In 3 the first attack occurred during pregnancy. No bacteria were isolated from the material obtained at biopsy or puncture of the nodules.

Ann. de dermat. et syph. 85: 385-411, July-Aug., 1958.

Tests for bacterial allergy showed that 5 patients had extreme hypersensitivity to tuberculin and seemed to belong to the group with Bazin's erythema induratum 4 had selective hypersensitivity to streptococci 2 to staphylococci and 1 to staphylococci plus Bacillus coli Thirteen showed no specific hypersensitivity In all patients with allergic sensitivity hypergammaglobulinemia was found The total globulins were often 75 80 Gm and the gamma globulin was usually over 17% in 5 it was over 20% In some cases there was hyperfolliculinuria The etiology does not appear to be uniform, but some cases definitely seem to have an allergic origin

The authors conclude that in apparently sensitized patients there is a whole gamut of lesions some known for a century e g Bazin's erythema induratum others for a long time e g erythema nodosum and others more recently described All have in common that (1) nodular lesions may appear and disappear rather rapidly without necessarily leading to ulceration (2) the lesions have a pathologic vessel at the center (3) the phenomena of necrosis are frequent and (4) the granulomatous reaction is secondary These conditions form an uninterrupted series of lesions from the most benign to the most serious which present at the beginning serious prognostic difficulties The allergic nature of these lesions is evident in Gougerot's dermic nodules and in some cases of nodular vasculitis it is very probable in periarteritis nodosa probable in many cases of erythema nodosum and of migrant thrombophlebiti

This idea is important because it permits an orientation of future work with regard to therapy—still uncertain—in these pathologic conditions which are increasing in daily practice

Postphlebitic Syndrome consists of progressive development of deep venous insufficiency and its complications It is caused by deep venous thrombosis in the pelvic veins or in those of the lower extremities This leads to edema development of collateral veins pigmentation induration especially above the medial malleolus a characteristic dermatitis and ulcer The incidence of postphlebitic syndrome is difficult to estimate Though many patients give a clearcut history of a deep venous thrombosis after childbirth injury operations infections diseases or prolonged immobilization as many have no recollection of such a vascular accident in the veins

A charleyhorse after bowling an ankle strain or a ruptured muscle treated by taping is often the beginning of a series of events leading to serious disability according to Geza de Takats* (Univ of Illinois)

Recanalization of the thrombus destroys the valves and leads to postural regurgitation Incompetent communicating veins freely transmit from the deep to the superficial veins the sudden rises of venous pressure during coughing lifting straining and sneezing Symptoms follow in a definite sequence from those of the initial thrombosis and subsequent bouts of periphlebitis through the stages of edema varicosities pigmentation dermatitis and induration to that of ulcer To prevent the long lasting recurrent disabilities seen in the later stages intensive treatment of the earlier stages is necessary

In the stage of incipient deep thrombosis there is calf pain cyanosis on dependency and some distention of the dorsal veins of the foot There may be minimal or no edema Inflation of a blood pressure cuff on the affected limb to 80-100 mm Hg produces severe pain Dorsiflexion of the foot evokes pain in the flexor muscles of the calf or in the popliteal fossa in about half the cases The affected calf is frequently warmer Treatment consists of hospitalization with the foot of the bed elevated and administration of heparin for 2 weeks The patient is ambulatory in 3 days and wears an elastic stocking for 6 10 weeks

In the later stages recurrent periphlebitis is treated by short intervals of intense elevation of the limb edema is controlled by elastic support and varicosities resulting from valvular insufficiency are treated by ligation and stripping

Wet dressings of aluminum subacetate solution Vioform* cream and hydrocortisone ointment have been found to be useful in treatment of dermatitis of the leg Early excision of plaques of postphlebitis induration is advocated Whenever possible the skin is saved but it must be removed if badly damaged In the early stages of ulceration ambulatory treatment with a glycerin gelatin cast may be successful After the ulcer is healed the induration is excised with or without grafting as indicated Palpation of the skin and its texture atrophy and obvious vulnerability are the best guides in deciding whether or not the skin covering the induration

* J A M A 164 1861 1 67 Aug 4 19 7

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Arilus cristatus is a reduviid of the order Hemiptera All Hemiptera have piercing mouth parts and are likely to be dangerous when handled The wing structure of this group differentiates them from the Coleoptera which are generally mechanically harmless beetles The distinctive feature characterizing the winged species of Hemiptera is the structure of their outer pair of wings which are thickened in the proximal portion and are membranous in the distal portion with overlapping of the wing tips Typical beetles differ in that the outer pair of wings are entirely chitinized hard and



Fig 31—A 1 t how g gwh 11k t long ted b d d tout p bosc (Court y f Smith F D t l A M A A h Derm t 77 3 4 330 M h 1958)

opaque meet in a straight line down the back and serve as wing covers for the membranous pair of wings underneath

The present case substantiates the generally accepted opinion that aside from pain serious or prolonged effects from the bites of Hemiptera are usually due to secondary bacterial infection or personal hypersensitivity

Kwashiorkor Report of Four Cases from Louisiana occurring in Negro children is presented by V Medd Hemington Edward Caroe Vincent Derbes and Barrett Kennedy* (New Orleans) Kwashiorkor is a protein deficiency disease first observed in equatorial Africa and since reported in various parts of Asia Europe and Central and South Africa The present cases are believed to be the first reported in the United States

The first patient aged 11 had continuous vomiting and diarrhea with passage of semiformed stools containing undigested food ascaria is profound inanition generalized edema associated with hypoproteinemia and anemia clinical

(*) A M A A h Derm t 8 157 170 A g t 1958

should be saved. After surgery the patient should never be without elastic support during the day, especially if sizable skin grafts have been used.

The author recognizes two indications for sympathectomy or repeated sympathetic blocks in patients with postphlebitic syndrome. When the leg is cold and clammy and shows diffuse vascular pain, repeated blocks or sympathectomy are useful. When the postphlebitic leg shows reflex hyperhidrosis and recurrent weeping eczema, sympathectomy dries the skin and helps healing of the resistant eczema.

Clinicopathologic Study of Skin in Mongolism.—David W. Kersting and Ionel F. Rapaport[9] demonstrated localized chronic hyperkeratotic lichenifications on the skin of 74.6% of 232 mongoloid patients. The lesions were clinically and pathologically consistent with lichen simplex chronicus. Some lesions showed a superimposed subacute eczematous reaction. Signs of excoriation were rare. In 90% of the group of mongoloids generalized ichthyosiform xeroderma was present. In patients in whom it was not present, usually younger mongoloids, eczema and lichen simplex had not appeared.

A characteristic feature of the mongoloid syndrome is generalized ichthyosiform xeroderma. Its cause is unknown. The authors believe that the generalized xerosis provides the abnormal dermal substrate for development of secondary eczema and lichen simplex chronicus.

Examination of 204 patients with cerebral palsy showed that 35% had some chronic lichenified eczema of the same type found in the mongoloids, a significantly lower incidence.

Insect Bite by Arilus Cristatus: North American Reduviid.—Francis D. Smith, Norman G. Miller, S. J. Carnazzo and William B. Eaton[1] (Omaha) report a case. The patient was a boy aged 10 months who had a painful but otherwise uncomplicated transient lesion. The insect is generally distributed over the southeastern two thirds of the United States and can be identified by a semicircular serrated crest resembling the edge of a cogwheel on the top of the thorax (Fig. 31). It has a three jointed proboscis or beak which is long and stout and when not in use is bent ventrally under the head.

(9) A.M.A. Arch. Dermat. [illegible]: 319-323, March, 1958.
(1) Ibid., pp. 324-329.

lermato es of kwa hiorkor are painless possibly in part be cau e of the apathy of the patients

Hypochromotrichia is characteristic Minimal changes in color involve the periphery and produce a halo effect Color ation may be light brown reddish golden gray or white Relapse may be reflected by the presence of striped hair

Skimmed milk has been most frequently used in the treat ment of kwashiorkor It is a convenient source of protein of high biologic value Small frequent meals should be given with a high proportion of milk and in the beginning ex tremely little fat If the patient requires treatment urgently the implest way to administer the necessary protein is by repeated tran fusions of packed red blood cells

[As pointed out here by Hennington and his co workers malnutrition is a worldwide problem and therefore kwashiorkor may be expected to occur in many parts of the world. Fortunately malnutrition is uncommon in the United States which must account in part for the fact that this is the first report of the disease from this country —Ed.]

Cutaneous Lesions of Rheumatic Fever Clinical Study in Young Adults During 18 month Orlando Canizares[3] (New York) ob erved 233 cases of rheumatic fever in an army air force convale cent center A special effort was made to de tect dermatoses po ibly related to rheumatic fever Those which could not be related were excluded from the study

Cutaneous changes due to the primary di ea e were ob erved in 24 patient (10 3%) The e included urticaria pur pura erythema nodosum subcutaneous nodules and ery thema multiforme There were 4 cases of urticaria In all ca e the appearance of wheals was related to exacerbations of the di ea e and to involvement of new joints Sedimenta tion rate was high As acute symptoms subsided urticaria di appeared Cases of urticaria easily traced to other causes uch a food were excluded

Four ca e of erythema nodosum were found with typical le ion on the anterior surface of the legs In each ca e the eruption appeared at the height of the articular involve ment when the edimentation rate was elevated and the P R interval long There were no relapses

Purpuric eruption localized to the legs and ankles oc curred in 5 patient The e le ions appeared gradually u u ally at the height of articular involvement although in 2 pa

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enlargement of the liver a reddish tinge of the ends of the hair, apathy and mental retardation and scaly follicular skin changes over the chest The fourth patient aged 20 month had vomiting ascariasis loss of weight generalized edema weakness and pronounced mental apathy Her hair did not show a reddish tinge but was lighter sparser and drier than usual Negroid hair The second and third patients aged 4 and 3 sisters of the first presented typical manifestation of kwashiorkor but in a milder (*forme fruste*) form All 4 children improved on a better dietary regimen

Diagnosis of kwashiorkor is made on the basis of the following manifestations (1) retardation of growth (2) dyspigmentation of hair and skin (3) edema usually associated with hypoalbuminuria (4) pathologic changes in the liver including fatty infiltration fibrosis and necrosis alone or in combination (5) nutritional dermatoses which may be absent or present in a variety of patterns (6) gastrointestinal disorders which may include anorexia digestive upsets diarrhea and mild steatorrhea (7) peevishness and mental apathy and (8) a high mortality if the condition is untreated or if it is incorrectly treated Differential diagnosis include pellagra cirrhosis of the liver and carcinoma of the liver

In mild cases there may be no definite dermatologic changes In advanced cases there may be severe dyspigmentation varying from bronze to reddish In white skinned children the first change is erythema which blanches on pressure This is rapidly succeeded by small purple patches which do not blanch Later they darken and have a waxy feel and sharp raised edge (enamel paint areas) These patches are scattered over the body but are most numerous over the legs thighs buttocks abdomen scapular region arms and forearms Within 2 3 days they change from their original florid color to dark brown reddish brown or black They become dry hard scaly and distinctly raised

While new areas of enamel paint dermatoses develop at the edge of the original lesion the central plaque enlarge Within a week regardless of treatment desquamation occurs The pale thin epidermis which is exposed may ulcerate if it does not the exposed areas feel smooth and oily In time there is repigmentation of the depigmented area of thin skin in which overlying enamel spots have been shed The

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Purpuric eruptions localized to the legs and ankles occurred in 5 patients These lesions appeared gradually usually at the height of articular involvement although in 2 pa

(3) A M A Arch Derm 6 0 0 December 1 5

tients they developed early in the disease The course of the eruption varied from 3 to 5 weeks

Three patients had subcutaneous nodules near affected joints After several weeks or even months the nodules slowly disappeared leaving no sequelae

Four patients had papular erythema multiforme The lesions were split pea size, dull red papules on the back of hands and feet and the extensor aspects of arms and legs They appeared gradually were asymptomatic and lasted 3-4 weeks Annular erythema developed in 4 other patients

The terminology of the ringed eruption of rheumatic fever in the literature is confusing To confine the term erythema annulare rheumaticum to the flat type and "erythema marginatum rheumaticum to the elevated type is impractical since many transitions can be found between the two types The term erythema multiforme rheumaticum (annular type) is suggested for this group

Granuloma Faciale Report on Case is presented by Madela H Foss[4] (Rikshosp Oslo)

Woman 38 was first seen in 1947 with a walnut sized bluish slightly elevated firm elastic tumor at the right mandibular angle (Fig 32) Similar but smaller lesions were located behind the left ear on the right ear on the upper lip and in the scapular region Histologic examination revealed acute inflammation of the skin but



Fig 3 —Tumor at right mandibular angle in 1947 (Court of F s M H Acta Dermat venereol 37 471 482 1957)

(4) Acta dermat venereol 37 471-48 1957

becau e of the clinical picture suggestive of malignancy the patient was treated with radium This was followed by chronic ulceration of the lesion at the angle of the mandible reduction in size of the le sion on the right ear and disappearance of the other smaller lesion

Healing of the ulcer due to radiotherapy of the lesion at the angle of the mandible occurred lowly and was followed by formation of a scar surrounded by an elevated bluish marginal zone which gradu ally increased in size during the next 10 years During this period the patient had constant pain in this area

In 19 7 the lesion wa 8X4 cm bluish to brownish red firmly ela tic well defined and involved the cheek in front of the right ear In the c nter there were cicatricial changes at the site of the previous radium application Smaller bluish nodules were present on the right side of the nose and at the opening of th right auditory canal

Biopsy of the marginal zone of the large plaque showed nodes of granulomatou ti sue rich in cell situated deep in the corium The infiltrate con iste l of many neutrophilic granulocytes and lympho cytes some plasma cells and eo inophilic granulocytes and slightly wollen pallid histiocytes Microscopic diagnosis was granuloma (probably granuloma faciale)

Granuloma faciale i usually asymptomatic and the pain in the present case is believed to have resulted from radio dermatiti rather than the granuloma itself Surgical removal of well defined plaques of granuloma faciale is sometimes successful but in this ca e surgical treatment does not seem indicated becau e of the size of the lesion and the probabil ity of poor healing in the treated area

Generalized Micropapular Dermatosis of Reticulofibrocyt ic Structure Accompanied by Specific Changes in Stroma (New Type of Cutaneous Reticulosis?) This report by St Gh Nicolau and L Balus[5] (Buharest) was stimulated by a recently published de cription of a similar case (Thiers *et al* 19) in which there was clerodermiform infiltration of the hand cutaneous infiltration of the face and confluent papu lar lesions of arms and thorax Histologically there was sig nificant proliferation with degeneration of elastic fibers ac ompanied by fibroblastic proliferation justifying classifi cation a a generalized diffuse fibroelastoidosis The authors believe that these 2 cases represent a new eruptive entity but they have u ed different terminology because their in terpretation of the condition differs from that of Thiers

Woman 3 ha l a generalized dermato i which had begun with a red li h s elling between the eyebrows and about 8 months later had exten led to other parts of the face the neck sternoclavicular regions

(5) A de mat et syph 88 146-156 M Ap 19 8

and extremities (Fig 33) At the beginning lesions consisted of isolated micropapules, and they coalesced later to become plaques of diffuse infiltration of a type almost sclerodermiform These lesions were of variable size As the eruption developed the skin began to thicken and become indurated Appearance of the skin disorder had coincided with appearance of the menopause The lesions of the face gave a peculiar appearance as if the patient were frowning There was no impairment of general health

Histologically the micropapular element consisted of a proliferation of reticular cells with an obvious tendency to become fibrocytic paralleling a sclerohyaline reaction of connective stroma

In considering the histologic characteristics of the infiltrate which mark the condition as a systemic disease the authors suggest that it may be a particular type of benign cutaneous reticulosis It is difficult to classify this case among known



Fig 33 Upper end of plaque on right upper arm showing granite appearance due to micropapular infiltrate Micropapules may be better seen in isolated lesions in left lower region recently invaded Multiple small areas of skin not involved due to vaccinal scar in center of plaque (Gay Prieto, Nicolau, S C and Bolus, J Ann dermat et syph 85 146 156 Mar Apr 1958)

types of cutaneous reticuloses in which presumably the initial cytologic type persists throughout the duration of the disease It is suggested that beside the classic orthoplastic reticulose there may be a metaplastic type characterized by transformation of reticular cells into fibrocytes capable of causing a sclerohyaline degeneration of the connective tissue stroma Clinically, this new type of reticulosis is differentiated from other types by the monomorphism of the eruption with micropapules which tend to coalesce to become a diffuse infiltration in the midst of which the papules are difficult to distinguish except at the edge of the plaque in areas recently invaded by the eruption

Miescher's Granulomatous Cheilitis with Multiple Cutaneous Manifestations Suggesting Lupus Erythematosus reported by X Vilanova J Piñol Aguadé and C Cardenal[6] (Barcelona)

(6) Ann dermat et syph 85 8 99 May J 1958

Boy 14 retarded physically and mentally w is examined on Oct 18 19 6 Four years previou ly red spots had appeared on the back of the hands and then on the fingers Almost simultaneously a deep h u e developed in the mucous portion of the upper lip which per sisted despite some improvement during the ummer months Insidi ou ly an l without acute inflammation or change in the general health the whole upper lip increa ed slowly in size an l numerous crevices appeared on its mucous surface

On examination the lip was double normal size The skin was lightly purplish and palpation showed total ela tic infiltration which extended to the nasal roots The red edge of the lip showed a deep me



F 34 (lym t heil t (Court y f V l X t l A n d m t et th 8 78 89 M y Ju 1959)

han crevice which extended to the gums There were al o other smaller fissures (Fig 34) covered by scabs of bleeding ulcerations Labial *muco a* and gum correspon ling to the region of both canines an l the 4 upper inci or were swollen an l presented a granular sur face covered partly by a diphtheroid p eudomembrane The tongue wa furr w e l Nasal muc sa w as covere l by sc abs an l a purulent exu lat which exten led onto the no trils

Le i n n the hand and finger were purpli h erythematou pots a lightly *ra ged* appearance (atrophic) covered by very fine and a lherent k quamation Submaxillary an l right axillary lymph glan l were swollen an l hard

Careful *general* neurologic endocrinologic and radiologic exam in ti n reveale l no other abnormalities Biopsies were made of the hypertrophic lip nasal *muco a* cutaneou lesions of hands and fin ger a well as a *stu ly of t* ue response to inoculation with living I C C ly cenification an l by intra lermal injection

A squamous erythematous lesion of the finger showed hyperkeratosis, accented in follicles and sweat gland pore Epidermal atrophy was present with only 2 4 layers of epidermal cells Interpapillary buds were extremely thin The dermis showed a diffuse infiltrate limited to the papillary body and formed only by lymphocytes and histiocytes At various points this infiltrate surrounded the basal layer and destroyed it The basal layer had lost its normal appearance, and in its place were epineural cells which here and there showed some necrosis There was mononuclear exocytosis at some point capillary vasodilatation with increase in size and number of endothelial cells and thinning of connective tissue and disappearance of elastic tissue in the area of the infiltrate edema was mild In the upper lip a large compressed infiltrate occupied all the dermis composed of histiocytes lymphocytes and some plasma cells with no polymorphonuclear cells In this infiltrate there were masses of epithelioid cell centered by multinuclear cell Connective tissue fibers and the elastic network were entirely dissolved in infiltrated region Tuberculoid formations were also found within the infiltrate

The patient was given streptomycin hydrazide vitamin D and prednisone without benefit Later with radiotherapy (450 r) edema induration and ulcers of the lip disappeared almost completely and the primary median fissure was treated surgically with good result Lesions on the hands improved progressively and at the last examination appeared merely hypochromic and slightly atrophic Lesions persisted in the ungual skin folds A small erythemato squamous lesion which appeared in the left ear disappeared spontaneously within a short time Around an old scar on the left side of the forehead a slightly erythematous poorly limited area had been noticed for several weeks with points of atrophy slightly rough to the touch and traversed by fine rare telangiectasias

Despite a clinical and histologic similarity to lupus erythematosus the authors do not believe that the lesions represent this condition They suggest the possibility of an extrafacial localization of a generalized or systemic disease in which granulomatous cheilitis is usually the major manifestion but which could be expressed also by other signs of pluri- oligo or monosymptomatic type

Eruptive Collagenosis with Multiple Foci and Metachromasia was observed by *J Gay Prieto P Rodriguez Perez* and *M Alvarez Cascos* (*Univ Skin Clinic Madrid*)

Man 44 was hospitalized because of skin eruption Examination revealed nodules of pinhead to millet size on the upper part of the body abdomen and thighs They were yellow and spheroid especially on the abdomen, and seemed to contain gelatinous material On the back thighs and upper arm the nodules appeared crowded formed a reddish yellow plaque were smooth and did not itch The mucous membranes appeared normal Blood study showed increased

(7) Hautarzt 9 300 304 July 1958

gamma globulins Itching disappeared on 250 mg cortisone daily X ray treatment to a small focus on the back failed

Histologic studies revealed that the nodules consisted of newly formed connective tissue cell The collagen fibers were swollen lightly basophil and difficult to recognize With silver impregnation the fiber net was well visible Metachromatic staining with toluidine blue and thionine showed a red stained substance between the collagen fibers of the nodules In fresh nodules the process seemed to begin with chromatic collagen changes Between the nodules there were two characteristic changes (1) minimal perivascular infiltration and (2) accumulation of numerous mastocytes giving the appearance of mastocytosis

The basic change seemed to be collagen transformation In support of this was the slight increase of globulins over albumin For this entity which has not been described yet the authors propose the name eruptive collagenosis with multiple metachromatic foci The disease also affects the glomeruli as seen in biopsy specimens Similar glomerular changes are found in acute lupus erythematosus

Familial Mediterranean Fever Harry Heller Ezra Sohar and Libby Sherf[3] (Tel Hashomer Government Hosp Tel Aviv) describe a heredofamilial syndrome occurring in persons of Mediterranean stock The disease is characterized by attacks of fever usually brief recurring at varying intervals and accompanied by pain in the abdomen or chest one or multiple joints or a combination of these regions In many patients erysipelas like patches of erythema appear on the lower extremities usually on the ankles or dorsa of the feet but occasionally on the calf Most of patients are non Ashkenazi Jews or Armenians In about 60% of cases the disease affects more than one member of a family Onset is almost always in the 1st or 2d decade

During abdominal crises pain is usually diffuse and soon becomes extremely severe Early the abdomen is somewhat doughy but later a boardlike hardness frequently develops In patients subjected to laparotomy during an attack gross pathologic lesions are absent Signs of improvement usually appear 6 12 hours after onset of an attack Chest pain is less common than abdominal pain It is located in the lower thorax usually on one side It is stabbing in character and intensified by deep breathing Usually decreased breath sounds at the lung base are the sole physical findings The attack subside after 12-48 hours Most patients with arthralgia

[3] A.M.A. Arch. Int. Med. 102: 0 71 July 1958

show redness and swelling of the involved joints Occasionally however no objective signs are present Even joints totally immobilized during an attack usually regain complete normal form and function immediately after the crisis Between attacks clinical examination is negative apart from possible splenomegaly Laboratory examination usually reveals a rapid sedimentation rate spherocytosis increased fibrinogen and in many cases proteinuria

Recovery has not been reported in familial Mediterranean fever Attacks may occur for many years sometime with remissions lasting several months Death in all cases has resulted from renal insufficiency At autopsy extensive amyloidosis is found Histopathologic investigations during life have revealed meager findings if any which can be regarded as specific

Nothing certain is known concerning etiology and pathogenesis No effective treatment exists ACTH and cortisone will not terminate or prevent attacks These drugs are believed by some to enhance deposition of amyloid material and their use seems contraindicated in this disease

The authors found many examples of this disorder in the literature It has been called by various names the best known of which are probably benign paroxysmal peritonitis and periodic disease The authors present data on 74 previously unreported cases The name chronic recurrent heredofamilial Mediterranean fever or in short familial Mediterranean fever is suggested

► [This article on familial Mediterranean fever is included in the Year Book because of the erysipela like patches of erythema of the lower extremities which may create confusion with other cutaneous syndromes

Heller et al believe that many cases of familial Mediterranean fever have been described under the heading of periodic disease but they feel that familial Mediterranean fever is not identical with the periodic disease described by Reimann (J A M A 136 239 Jan 24 1948) which is not associated with cutaneous manifestations such as angioneurotic edema and purpura —Eds]

Parapsoriasis Varioliformis and Its Histology was studied in 5 cases in which 21 biopsies were made by J Piérard (Gent) and E P Van Steenbergen (Utrecht) [9] In this condition along with papulo and maculo squamous lesions of parapsoriasis there are purpuric hemorrhagic lesions papulovesicles or papulopustules and blackened scab covering small necrotic ulcers Systematic study of these varied lesions

(9) Ann dermat et syph 84 630 646 Nov Dec 1957

demonstrated successive stages from the squamous papule to the vesicular element or to loss of substance characteristic of parapsoriasis varioliformis which is followed by an atrophic scar

One patient had acute parapsoriasis varioliformis which lasted 3 months and 4 had a more chronic course which presented all varieties of the multiform lesion

CASE 3—Indonesian man 26 had a skin eruption which had begun 3½ months before in the axillae and popliteal creases and had extended within a few weeks to the trunk and extremities (Fig 35) At the beginning there was a small papule covered with a vesicle When these dried up there was pronounced itching Examination revealed an exanthema scattered symmetrically on the neck trunk arms composed of various lesions (1) rounded lenticular red brown papules with a violet center (2) macules with a central scab (3) larger lesions 4 6 mm in diameter red and papular some with a livid elevation at the center resembling a blister and others with a slightly depressed necrotic scab (4) numerous pigmented spots 3 4 mm with central atrophy

The changes produced by the varioliform process in the initial histologic lesion of parapsoriasis guttata are evidenced principally in increased abundance of intraepidermal edema with a tendency to cavity formation the epithelial cellular changes leading to necrobiosis (Fig 36) presence of vascular lesions and diapedesis of numerous blood cells As edema increases and the lesions become more complex with lacunae more numerous and voluminous fusion of these cavities gives rise to the vesicles containing epithelial cells in various stages of degeneration and cellular and nuclear debris of lymphocytes red cells and some polymorphonuclear cells and fibrin filaments These changes occur along with obvious lesions of epidermal cells edema homogenization of protoplasm with disappearance of reticular structure cavitary change and polymorphous degeneration of nuclei The final result is death of the cell which may be transformed into hyalin or be completely lysed In the extreme stage the entire epidermis is necrosed with the papillary dermis and this gives rise to formation of a layered scab consisting of debris of all involved cellular elements Vascular lesions begin with congestion progress to infiltration of the wall and in necrotic stages its destruction These vascular changes explain the presence of red blood cells in superficial and middle dermal layers which may be seen even





Fig 35 (t p) —Parat [illegible] l f [illegible]

Fig 36 (b tt m) Sect [illegible] m f p d n [illegible] t [illegible] tw [illegible] uper n p [illegible] ed [illegible] Upper (dark) re ult f n cr [illegible] [illegible] tely bel w l ght band is [illegible] ege erated ep [illegible] n [illegible] tt ck [illegible] inflammat y proce [illegible] parap [illegible] ia is variol [illegible] vil [illegible] nt [illegible] e f s [illegible] ll a te an [illegible] ft dermoepid rmal bo [illegible] de n [illegible] c ll ken [illegible] (C urte [illegible] f Liera [illegible] J an [illegible] Van St [illegible] Ann dermat [illegible] s ph 84 630 646 No De 1957)

in less differentiated lesions When a histologic section resembles that of parapsoriasis guttata with pronounced cellular changes in the epidermis and red blood cells in the dermis parapsoriasis varioliformis should be suspected The classic lesions of parapsoriasis guttata pass almost imperceptibly into the more varied and eventually completely different lesions of parapsoriasis varioliformis

Unusual Case of Dermatitis Factitia is reported by Abraham Zelony[1] (Patchogue N Y)

Woman 59 and obese psychiatric patient who refused to answer questions was referred for dermatologic consultation with a tenta



Fig 37—Le mea n g 8 mm on bd men (C rt f Z lony A M A A h D m t 8 398 399 S pt mbe 195)

tive diagnosis of petechiae of undetermined origin There were 12 15 round violaceous slightly depressed atrophic lesions on the abdomen (Fig 37) Numerous scattered small firm intradermal and subdermal nodules were palpable in the skin of the abdomen Many of the nodules were not associated with the visible lesions Because the lesions were not truly petechial and did not fit a pattern associated with a specific dermatitis a diagnosis of dermatitis factitia was entertained

When attempting to biopsy one of the lesions the cutting instrument touched a rigid object with a metallic click A small hemostat was then used to remove an ordinary sewing needle An x ray (Fig 38) confirmed the impression that the other lesions were also caused by similar foreign bodies Apparently most of the needles were in

(1) A M A Arch Dermat 78 398 399 Sept be 1958

50μ

Fig 35 (top) Pa ag [illegible] a ol f [illegible]

Fig 36 (l tt) — Sect n f [illegible] m [illegible] nt [illegible] tw [illegible] peran po ed l et Upper (da k) re ult f nec b [illegible] l oc [illegible] f el [illegible] at [illegible] Immed tely bel w light band i regenerate l ep de n [illegible] tt ke l n t [illegible] fl m t y proc of parap rasi var l f rm e le t n nt e [illegible] f s ll a t s and ft dermoep dern al t r le [illegible] we l k l t ep nt l nal ll ge

(C urte y of Tier rl J [illegible] nl V n St nt gen F [illegible] Ann d mat t o ph 84 630 646 Nov Dec 195)

left hard From time to time man pieces of white chalky material discharged through the skin co er ng the masses Se en years ago she noticed the gradual appearance of a similar but larger mass just be neath the skin of the lateral su face of the middle third of the left leg Shortly after an attack of uperfic al phlebitis of the left leg 2 years ago a small piece of ha d hite material discharged through tl kin of the leg Healing was prompt but a econd piece of chalk lis harged 22 m nths lat r This time an ulcer formed at the site of



(Cou f R J b Brit J D rm t 70 107 109 M h 19 8) Fig 39 Fig 40

l charge Examination revealed gross internal saphenous veins with tem of the lower two thirds of the left leg On the lateral a pect there was a reddish area containing 3 small sinuses (Fig 39) Be neath each sinu a hard plaque could be felt and on looking down a inu a white chalky material could be seen beneath the kin This wa ra liopa que (Fig 40) The olar surface of 3 fingers of the left hand contained several mall radiopaque deposit similar to that in the leg Juxtafemoral l gation of the left internal saphenous vein was performed and the calcareou concretion was removed from the ul er Ela tic adhesive ambulatory compression was used and the ulcer healed in 4 weeks

► We have had und r our care a woman with a chronic dermatitis of the lower extrem ties and an in lol nt ulcer on one hin which had failed to



Fig. 38.—X-ray of abdominal region showing presence of numerous foreign bodies. (Courtesy of Zelon: A.M.A. Arch. Dermat. 78:398-399, September 1958.)

serted with no visible skin changes resulting. In a few instances the chronic trauma of the skin by a needle not as yet completely walled off by fibrous tissue resulted in a localized area of atrophy. The atrophic skin was pigmented from hemosiderin which appeared after injury to the capillaries.

► [This is one of the very unusual cases of factitious dermatitis which are reported from time to time. No such thing here as looking for *one* needle in the haystack!—Eds.]

Calcinosis Circumscripta Presenting as Varicose Ulceration. Calcinosis circumscripta is a rare condition occurring mainly in women of middle or advancing years, who show scattered calcareous, radiopaque concretions in the subcutaneous tissues about the joints of the upper and lower extremities and pelvis. The cause is unknown. Stanley Rivlin (London) presents a case which appeared as varicose ulceration.

Woman, 63, had had varicose veins for 20 years. Thirteen years ago she became aware of small, hard lumps in the pads of 3 fingers on the

(2) Brit. J. Dermat. 70:109, March 1958.

gave a marked reaction for phosphates with Ko sa s stain and ap peared to be calcification

CASE 2 — Miner 21 had groups of small white papules arranged in a line on the left elbow He had probably abraded the elbow be fore on et of the eruption but he could not remember a particular injury The histologic picture w is not identical with that seen in Case 1 since there was a break in the epidermis and the gap was filled with metachromatic structureless material which did not stain completely with Kossa s reagent

Both patients worked in a section of the mine where roof water containing 3 5% calcium chloride dripped on them This water appeared to be the cause of the cutaneous lesions Similar lesions were produced experimentally on the skin of one of the authors by applying 3 5% calcium chloride solu tion to a scarified area on the forearm (Fig 41) for 72 hours The experimental lesions cleared in 6 weeks the miners re covered in 4 months

► [An interesting series of events The authors speculate on the possibil ity of such a mechanism playing a role in the formation of renal calculi —Eds]

White Lesions of Vulva Discussion of Lichenification (Lichen Simplex Chronicus) Leukoplakia Bowen s Dis ease Kraurosis Vulvae" Lichen Sclerosis et Atrophicus and Senile and Essential Atrophies of Vulva is presented by Arthur B Hyman and Henry C Falk[4] (Beth Israel Hosp New York) Lichen simplex chronicus leads to a thickening of the skin with increased skin markings better appreciated in the groin and on the pubis and thighs than on the labia majora The outlines are usually less well defined than the plaques of leukoplakia and the color is brownish or ery thematous rather than dead white Leukoplakia is essential ly a di ease of the mucosa or mucocutaneous tissue The skin around plaques of leukoplakia may show lichenification due to long continued scratching Erosions ulcers or keratoses in leukoplakia are warning signals of the possible interven tion of malignancy but erosions in lichen simplex chronicus re ulting from scratching do not indicate possible carci nomatous change

The rough verrucous outstandingly hyperkeratotic le sions found in most cases of Bowen s disease of the vulva (and in Paget s disease) should make it easy to recognize that more than just lichenification is present Bowen s dis ease is particularly a disease which afflicts older adults and

(4) Obst & Gynec 12 407-413 Oct be 1958

heal under many forms of therapy It was not until calcareous deposits at the base of the ulcer were dissected out under local anesthesia that the ulcer eventually healed These deposits had been shown on x ray to be linear and associated with nonfunctioning vessels in the area they were diagnosed as calcified phleboliths and calcifications of the veins —Eds]

Traumatic Calcinosis of Skin I B Sneddon and R McL Archibald[3] report 2 cases

CASE 1—Coal miner 29 had an eruption on the back which appeared 3 weeks after the back was abraded while he was working in

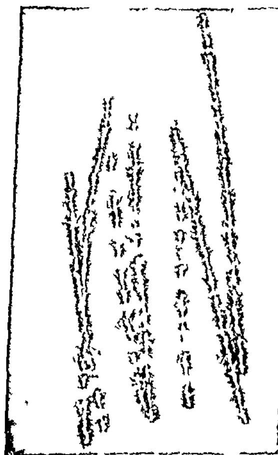


Fig 41—Experimental lesion produced by calcium chloride solution (Courtesy of Sneddon I B and Archibald R McL Brit J Dermat 70 11 14 Jan 1958)

the mine The eruption consisted of firm white papules 2 3 mm in diameter some in ring formation and others linear Most were surrounded by an erythematous halo They occurred at the exact sites where the skin had been abraded Histologic examination showed an intact and normal epidermis In the upper dermis was a zone which

(3) Brit J Dermat 70 11 714 June 1958

enification Grenz rays and thorium X are safer Antipruritic applications are useful for symptomatic relief in leukoplakia Sometimes spontaneous improvement occurs Vulvectomy should be performed only if there is evidence of malignancy or impending malignancy It is the recommended operation for Bowen s and Paget s diseases Lichen sclero is et atroph icus shows symptomatic relief with antipruritic agents and a trial with chloroquine orally is worthwhile Essential tightening of the introitus may be helped by dilators Estro gens by mouth or locally are not beneficial in any of these vulval diseases

► [To the cond tions listed here which might produce whitish lesions of the vulva one could add lichen planus and moniliasis We agree with the authors that kraurosis vulvae has become such an ill-defined and hazy concept that it might be best if the term was abandoned Dermatologists have always been alert to the various conditions which are seen on the vulva and have differentiated between those which are precancerous and those which have no malignant potential Unfortunately others on occa sion have failed to make these differentiations and have done vulvectomies in cases of harmless vulvar dermatoses Hyman and Falk s article should be helpful in remedying this situation —Eds]

Steatocystoma Multiplex with Embryonal Hair Forma tion Case Presentation and Consideration of Pathogenesis Miguel A Contreras (Ciudad Trujillo Dominican Republic) and Maurice J Costello (New York) report 3 cases of stea tocystoma multiplex in which multiple embryonal hairs grouped in bru hlike arrangement were found in typical cysts The hairs were similar to those found in trichostasis spinulosa which the authors believe is a congenital malfor mation probably related to steatocystoma multiplex

With regard to the pathogenesis the question arises whether the cysts of steatocystoma multiplex are retention cysts or cysts of new formation belonging to the atheromas or a nevoid condition Opinions vary The finding of multiple hairs in the cysts seems to favor the atheromatous nature

Against the theory of retention cysts are the facts that the cysts are congenital (some patients are born with them) and familial They are inherited according to mendelian law and often are accompanied by other malformations in the pa tients or their families They are rare or absent in patients with severe cystic acne The presence of fully developed com edones and acne vulgaris in patients with steatocystoma is al o rare The cysts are symmetrically distributed It is dif ficult to demonstrate the occluded sebaceous duct which in

(3) A.M.A. Arch De mat 76 720 25 Decembe 19 7

it may involve the skin as well as the mucocutaneous tissue

Lichen sclerosis et atrophicus of the vulva involves skin and mucocutaneous tissue The size of the labial adnexa and introitus may be normal or contracted The tissue covering them and the vulva as a whole is thinned the periphery of the diseased areas is usually well defined and outlying flat topped atrophic papules may be seen The cigaret paper wrinkling of the surface of affected sites is characteristic Itching is prominent so lichenification is apt to be an as o ciated feature Classic lesions of lichen sclerosis et atrophicus may be found on other areas of the skin

In purely senile changes of the vulva the introitus is not narrowed The labia shrink and are absorbed Unless com plicated by other conditions there is no pruritus or other symptoms

Narrowing and tightening of the introitus usually with diminution or disappearance of the labia but without thin ning of the skin are a rare combination that may be found at all adult ages Patients usually come for consultation be cause of dyspareunia or difficulty and pain on insertion of a pessary Very little is known about this group These ca e are the only ones for which the term kraurosis vulvae (es sential narrowing of the introitus) is justifiable It is pos sible that they belong to the group of scleroderma

With a good clinical history and clear indication of the bi opsy site leukoplakia and lichenification may be distin guished microscopically but without these histologic diag nosis is largely guesswork The most important histologic finding in Bowen s disease is the great variety of cell and nu cleus types found within the epidermis The microscopic pic ture in lichen sclerosis is characteristic Senile vulval changes seldom show striking features Atrophy is more definitely recognizable clinically than histologically The authors believe that cases reported as kraurosis vulvae with a histologic picture of lichen sclerosis et atrophicus are actu ally examples of the latter disease They consider it untenable to distinguish between kraurosis and *lichen sclerosis* on the basis of changes in the vessels of the deep cutis In any of the above conditions when radiation has been used it may be *impossible* to unravel the histologic effects of radiation from the microscopic features of the disease proper

The authors advise against repeated x irradiation in lich

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(5) A.M.A. A ch. Dermat. 76 720 725 Decembe 1957

most instances is not present The cysts contain nonoxidized fat in contrast with the oxidized fat in retention cysts They sometimes occur on the palms and soles where the pilosebaceous glands are absent On the basis of the findings in their cases the authors favor the hypothesis that the cysts are of new formation on a nevoid basis

Fox-Fordyce Disease with Hidradenitis Suppurativa Pore closure is a feature of both Fox Fordyce disease and hidradenitis suppurativa It might be logical to suspect that the two diseases would often be found together, but Rachel Ford Spiller and John M Knox[6] (Baylor Univ) found only 1 report of hidradenitis suppurativa as a complication of Fox Fordyce disease in the English literature They present 3 cases in which the disorders occurred simultaneously

Negro woman 33 had deep painful, nodular lesions in the axillae Many small flat topped papular lesions were present in the axillae about the nipples and in the vulvar region These lesions were extremely pruritic and had been present 10 12 years The hidradenitis suppurativa responded promptly to therapy The pruritus associated with Fox Fordyce disease was relieved by oral Terramycin® but various forms of treatment including vitamin A antihistamines Gantrisin® and topical hydrocortisone had no objective effect on the papular lesions

Pathologic examination showed the stratum corneum to be irregular with alternate areas of normal thickness and hyperkeratosis In some areas there was pore closure with keratinous plugs in the ducts Underlying the plugs the ducts were dilated and surrounded by intra and intercellular edema The rete ridges were elongated and broadened The superficial dermis was normal Deeper there were many foci of inflammatory cells primarily about eccrine and apocrine glands A large abscess was present in the deep dermis

The superficial histopathologic changes in this case were those of Fox Fordyce disease and manifested clearly the classic sweat retention vesicle near the pore outlet The large abscess in the dermis was nonspecific but characteristic of those found in hidradenitis suppurativa The anatomic location of obstruction or the presence of secondary infection may determine whether Fox Fordyce disease hidradenitis suppurativa or both develop in a given patient

Perianal Hidradenitis Suppurativa Clinical and Pathologic Study is presented by Markham J Anderson Jr and Malcolm B Dockerty[7] (Mayo Clinic and Found) Of 117 patients with perianal hidradenitis suppurativa 65% were

(6) J Invest Dermat 31 127 135 Aug t 1958
(7) Dis Colon & Rectum 1 23 31 Jan Feb 1958

males The perianal region is involved in about 1 of every 6 cases and is the only site of lesions in 1 of every 13 cases Hidradenitis may also involve the neck face calp extremities shoulders and abdomen

Anal fistula secondary to hidradenitis is rare Hidradenitis in the postsacral area is easily confused with pilonidal disease especially if other parts of the body are not involved The term perianal hidradenitis is used rather loosely since many patients with disease in the anal region also have involvement of the scrotum buttocks proximomedial aspects of the thighs and the inguinal and pubic regions A line of demarcation usually does not exist between the anal involvement and that of other regions

The cause and pathogenesis of hidradenitis suppurativa are not well understood Study of the 261 sections taken from the surgical specimens in 64 patients disclosed that eccrine glands were present in 59 whereas typical apocrine glands were identifiable in only 7 The apocrine sweat glands apparently are not of great importance in the pathogenesis of the disease their involvement appears to be coincidental The disease seems to have some relation to endocrine activity and it is likely that common etiologic factors are present in hidradenitis and acne Other than the presence of apocrine gland local conditions exist that might help explain the typical distribution of hidradenitis suppurativa Among these are the frequent apposition of cutaneous surfaces excessive local moisture heat and friction and the difficulty of maintaining cleanliness in the regions frequently involved

Treatment of hidradenitis of the perianal region is somewhat discouraging because many patients continue to have recurrences even after careful excision of all active sites Until the cause and pathogenesis are better understood it is doubtful that prognosis will improve

► [The finding that *only* eccrine glands were present *in* 57 of the 64 cases which were studied histologically *seems* to contradict accepted concepts of the role of apocrine glands in hidradenitis suppurativa It is difficult to follow the reasoning of the authors when on one hand they say that apocrine glands apparently are not of great importance in the pathogenesis of the disease (hidradenitis suppurativa) and on the other they suspect that hidradenitis and acne have common etiologic factors such as endocrine effects Actually such a concept would *relate* the sebaceous and apocrine glands as it is well known that the pilosebaceous unit (and not the sweat glands) which is the shock tissue for acne is definitely influenced by certain hormonal changes and that the apocrine glands are also

most instances is not present The cysts contain nonoxidized fat in contrast with the oxidized fat in retention cysts They sometimes occur on the palms and soles where the pilosebaceous glands are absent On the basis of the findings in their cases the authors favor the hypothesis that the cysts are of new formation on a nevoid basis

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(7) Dis Colon & Rectum 1 23 31 Jan F b 1958

Unusual Manifestations in Case of Relapsing Nodular Febrile Panniculitis (Weber Christian Disease) are reported by Leonard M Goldberg and Leonard W Ritzmann[9] (VA Hosp Portland Ore) The patient a man 39 had manifestations considered diagnostic of Weber Christian disease—a chronic febrile illness with recurrent subcutaneous inflammatory nodules that histologically showed the classic picture of fat necrosis and in healing left atrophy pitting and hyperpigmentation of the skin In addition several aspects of the disease were considered unusual Every lesion that appeared followed trauma In some instances the trauma was relatively insignificant One cutaneous lesion appeared in an area where the patient had lain on a hard object another occurred from a blow on the leg with a reflex hammer The lesions often underwent liquefaction Although the inflammatory process of Weber Christian disease is classically considered to be unassociated with fluctuation Weber s second patient and the patients of several other authors showed suppurative inflammation

Another unusual feature was extensive bone involvement Serial x rays showed the evolution of a typical protrusio acetabuli after a fall 9 years ago It is assumed that the trauma of the fall produced inflammatory necrosis in the synovial fat of the acetabulum This severe inflammatory condition then destroyed the acetabular floor On another occasion the patient twisted the right knee The knee became hot red and swollen and aspirations yielded a greenish gray sterile pus On other occasions minor trauma resulted in swelling of both knees and right ankle Early radiographs of the right knee showed demineralization of the distal end of the femur and proximal tibia Serial films showed a return of calcium but in heavy coarse irregular striations differing from the recalcification after demineralization of bone from disuse The coarse irregular trabeculations could have resulted from recalcification of areas of bone underlying an inflammatory process in the synovial fat Myocardial infarction also occurred on the 5th day of hospitalization after a syncopal episode with no apparent cause The ECG abnormalities were more acute than would be expected if the myocardial infarction had precipitated the syncopal attack 5 days previously

(9) Am. J M d. 25 88-95 N embe 1958

influences by these changes To our knowledge the eccrine glands play no primary role in the pathogenesis of either of the diseases —Eds]

Spontaneous Chronically Relapsing Panniculitis was observed in 2 men by A Fanninger and M Isvaneski[8] (Zrenjanin, Yugoslavia) The disease lasted for 10 and 6 years respectively In both patients the nodes developed continuously during the entire year In 1 patient the intensity of the disease increased in spring accompanied by general malaise

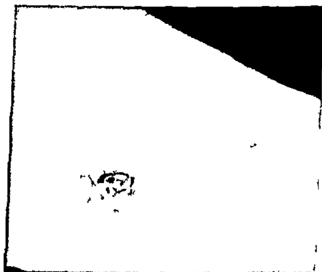


Fig 4 —Boat shaped retraction of closed and ulcerated nodes of left leg (Courtesy of Fanninger A and Isvaneski M Hautarzt 9 372 4 August 1958)

Remissions lasted 1 2 months The nodes evolved in about 20 days The end of their regression was characterized by a boat shaped retraction from the skin surface (Fig 42)

The nodes which ulcerated occasionally were hazel to walnut sized painless and adhered to the skin They were localized mostly on the limbs but were seen also on the trunk Histologic studies revealed granulomatous infiltrations The patients studied showed the symptoms of Pfeifer Weber Christian and of Rothmann Makai diseases

The authors suggest that the diseases with spontaneous panniculitis be considered as a uniform group and that the forms seen in the patients studied and those described by Rockl and Thies be interpreted as transitory form between Pfeifer Weber Christian and Rothmann Makai diseases

(8) Hautarzt 9 372 374 August 1958

cally with intracutaneous injection of saliva antigens prepared by the authors

► [The concept of aphthosis or Behçet's syndrome has been steadily widening. It now encompasses not only the mucous membrane, ophthalmologic and genital changes originally included but also other cutaneous and neurologic lesions. The word aphthosis actually mean a disease consisting of small defects of the mucous membrane. This is hardly a good term for the nodular lesions in the skin and the neurologic alterations. However for lack of a better one the term aphthosis can be retained at least until more becomes known about the cause of this disease.

Much more work seems required to ascertain the significance of the 2-3 week reactions in skin tests with saliva antigen. The specificity of this test can only be established by further controlled studies. Another skin test in aphthosis using a suspension of material from an active lesion was suggested by Franceschetti and Jadassohn. Here, too, the specificity of the skin test has not yet been firmly established.—Ed.]

Acrokeratoelastoidosis is discussed by Ismael M. Fompostello and Santiago J. Mosto (Buenos Aires) with 4 case reports. Since Castro's original description in 1952 only 4 more cases have been reported. The authors believe, however, that the condition is not uncommon but that it is classified under other less accurate diagnoses. Any diagnostic difficulty with regard to this lesion is due to lack of knowledge concerning it. The three characteristic features are papulokeratotic lesions, distribution on the hands and feet and attenuation and fragmentation of elastic fibers microscopically. Biopsy also shows marked acanthosis with hyperkeratosis and granulosis. In the papillary dermis connective tissue fibers are enlarged and discretely *homogenized* with dislocation in the deeper layers forming a network. All cases so far observed have been in women.

Ages of patients in the present series were 42, 27 (2 patients) and 35. Lesions occurred on the external and internal borders of the palms and soles in all. In 1 patient the joints of the fingers and the thenar and hypothenar eminences were also affected. Single papules were 2-4 mm. in diameter. They were *rounded* and assumed a polygonal shape in areas where they united to form small plaques. The papules were slightly elevated, smooth and white, yellowish white or the color of normal skin. Palpation revealed a certain keratotic resistance. Lesions could be observed more clearly with pressure or by stretching the skin between the thumb and index finger. This delimited a plaque of whitish papules. In 1 case single lesions were distributed in a ring like a rosary. In no case were there any subjective symptoms. The dermatosis was

(2) A h gent. 3 mai 7 72 7 S pt mbe 1957

The authors suggest that when the patient fell during a fainting episode there may have been sufficient trauma to the pericardial fat to result in inflammatory fat necrosis The inflammation could have caused a contiguous angiitis of a coronary vessel traversing the area with a resultant inflammatory occlusion and myocardial infarction A mild fever noted during the first few days of hospitalization could have represented the usual febrile reaction to the patient s panniculitis rather than myocardial necrosis

Nodular Aphthosis, Aphthose en Plaques and Pfeifer Weber Christian Panniculitis Experimental Reproduction of Nodular Lesions in Aphthosis X Vilanova and J Pinol Aguade[1] (Univ of Barcelona) studied 6 patients 4 men and 2 women aged 24 64 with nodular vasculitis a syndrome belonging to the disease group of aphthoses One patient showed symptoms and signs of the Pfeifer Weber Christian syndrome All patients but 1 had the nodules on the lower extremities In this patient the cutaneous infiltration appeared as a large plaque in the face This form of recurrent infiltration which leaves a depression in the affected area has not been observed in aphthosis so far

The histology of the nodules was not uniform probably because the biopsies were taken from nodules of different developmental stages The nodules showed besides fibrinoid degeneration a proliferation of the connective tissue cells of the corium The latter was of tremendous extent only in the plaque shaped facial infiltration observed in 1 patient where the entire corium was acutely inflamed with considerable involvement of polynuclear cells giving the appearance in some areas of early suppuration Generally the fibroblastic and histiocytic proliferation was not pronounced in the pericapillary histiolymphocytic infiltrations The arterioles and medium sized veins may be involved and symptoms of panvasculitis may be present The capillaries may be dilated and thrombosed The subcutaneous tissues react late and form a lipophagic granuloma These characteristics allow differentiation from erythema nodosum from tuberculous and nontuberculous nodular vasculitis and from the various forms of panniculitis

The nodules could be reproduced clinically and histologi

(1) Hautarzt 9 389 398 September 1958

was some indication of cavity formation in a few sudoriparous glands and the epithelium was flattened

Large doses of vitamin E orally and 3 applications of carbon di oxide snow at 1 week intervals healed the lesions almost completely leaving a pink slightly atrophic thin and smooth skin

The clinical aspects and histologic findings conformed to those of elastosis described by Favre and Racouchot except for the age factor The atypical young age of this patient and of another sailor with the same condition seen but not treated by the author suggests the hypothesis that the external trau matizing factors such as climate heat and sun to which these sea going persons were exposed must have acted on a skin that was already predisposed to early senescence

► [An essentially identical clinical picture as that described by Sprecher was reported by Berlin (A.M.A. Arch Dermat. & Syph 69 683 1954) as due to paraffin oil in hair preparations We have since seen several patients in private practice presenting a similar picture each of whom had used hair dressings containing petrol tum or petroleum oils—Eds]

Dyskeratosis Ichthyosiformis Congenita Migrans Variant of Congenital Ichthyosiform Erythroderma In 1949 under the name ichthyosis linearis circumflexa Comel described a clinical picture characterized by slowly extending serpiginous and polycyclic lesions hyperkeratosis of the flexures and hyperhidrosis of the palms present from birth Danilo V. Stevanovic and Radoslav L. Pavic[4] (Univ of Belgrade) found only one other report of this dermatosis in the literature They report another case with features identical with those previously reported with the addition of the occasional development of flaccid bullae

Youth 20 had red scaly skin at birth and since then the skin had never been completely normal On the trunk and extremities were many annular and polycyclic lesions of various sizes with slightly raised edges (Fig 44) On the forearms and legs there was slight desquamation in addition to these polycyclic lesions Two flaccid bullae were noted in the groin In the axillae and in the popliteal and antecubital flexures the skin was hyperkeratotic and slightly brown The palms and soles showed hyperhidrosis The scalp was covered with greasy scales Microscopic examination of a thigh lesion showed thickening of the epidermis a loose horny scale and parakeratosis In the papillary layer the vessels were slightly dilated and there was an infiltrate of lymphocytes and histiocytes mainly perivascular There was mild interstitial edema throughout the dermis

The authors believe this condition is a variant of ichthyosiform erythroderma Both dermatoses are present at birth or soon after and conspicuously involve the flexures Both show

(4) A.M.A. Arch Derm. 73:5 ... 9 ... be 19 8

discovered casually because of its localization on the hands

Cutaneous Nodular Elastosis with Cysts and Comedones A Sprecher[3] (Genoa Italy) reports the results in his study of 1 case

Man 24 stoker on board ship thin but in good general condition had noticed 6 months before the sudden and painless onset of black comedone like *raised points on the temporozygomatic regions* (Fig 43) bilaterally and symmetrically The lesions increased progressively in volume and number and when squeezed yielded a whitish *rather dry substance* Between the comedones was a limited num



Fig 43 (Courtesy of Sprecher A Minerva dermat 33 314 319 August 1958)

ber of nodular formations the color of pale healthy skin millet sized and firm The skin surrounding and between the lesions appeared healthy although it had the characteristic appearance of skin of sea *going* persons Clinical and laboratory tests were normal

Histologic examination of skin from the right temporal region showed a thin atrophic epidermis with all the various layers thinner and poorly *differentiated* The superficial dermis had vast areas of degenerated substance in clusters constituting the common reticular structure of the tissue and interspersed with zones of normal or almost normal tissue in which elastic fibers and fibrils were visible The deep dermis was more compact with homogeneous fibrinoid degenerations *similar to those* of granuloma annulare in some points Hyaline or amyloid degeneration and mucopolysaccharide were absent All the specimens showed numerous isolated cystic formations some closed some *communicating* with the outside through a follicle often attached to stumps of pilosebaceous system to which were connected normal or more often atrophic sebaceous glands There

(3) Minerva dermat 33 314 319 August 1958

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(4) A M A A h D rm t 8 625 629 N mbe 1958

pruritus hyperhidrosis of the palms and seborrhea of the scalp The occasional presence of bullae in the authors patient is another feature observed in both syndrome The histologic changes in the patient reported are compatible with this assumption Hyperkeratosis of the palm and soles often found in ichthyosiform erythroderma has not been found in this syndrome Because of the striking config

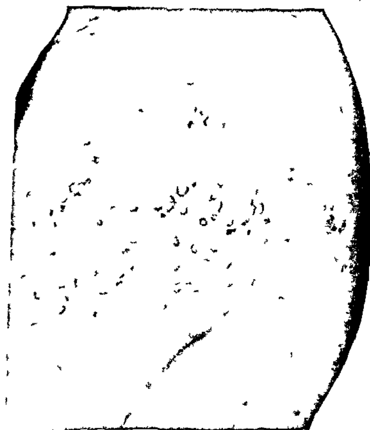


Fig 44—Annular and p lycycl les on of left h uld (C urte y f Ste ano c D V and Pavic R L (M A Arch D rm t 8 6 5 6 9 No ember 1958)

uration of the lesions and their progressive extension and the general similarity of the syndrome to ichthyosiform erythroderma the term dyskeratosis ichthyosiformis congenita migrans is suggested

► [Apparently no fungous examination was done on the serpiginous and polycyclic lesions In at least 1 case of congenital ichthyosiform erythroderma it was possible to explain the polycyclic and serpiginous lesions on the basis of superimposed superficial fungous infection (Arch Dermat & Syph. 56 834 1947) Perhaps the same mechani m was operative in the patient of Stevanovic and Pavic—Ed]

Isolated Dyskeratosis Follicularis James H Graham and Elson B Helwig[5] (Armed Forces Inst of Pathology) studied 50 examples of the isolated lesion removed from persons aged 22 67 none of whom had more than 1 lesion The average duration of the lesion was 3½ years Most lesions were about the head and neck Clinically they were usually confused with cystic lesions senile keratosis or basal cell carcinoma

The lesions were single elevated nodules or cysts with



Fig 45—B se f le on f sol ted dy k rat f llic l h wi g basal ll hyperpla ia p p ll m tos d la fill d w th a th lyt d dy k tot c lls. Les on ah rply dem ted from ou d g m ed ed f om 115 (Cou t y f C h m J H and H l g E. B A M A. A h D mat. 77 377 389 April, 1958)

raised borders and somewhat umbilicated or porelike centers Most were brown but some were flesh colored yellow red black tan or gray They were firm circumscribed rough and granular to palpation Drainage crusting and bleeding were common and local itching pain or a burning sensation were the usual symptoms

The specimens were contributed with various pathologic diagnoses Keratosis follicularis was the diagnosis in 10 carcinoma in 15 and in 9 the diagnosis suggested origin from eccrine or apocrine sweat gland A diagnosis of isolated Darier's disease was made in 2 cases

Examination under low power revealed a sharply circum

(5) A.M.A. Arch Dermat 77 377 399 April 1958

scribed cup shaped enlarged follicle extending deep into the underlying corium Usually a keratotic and parakeratotic plug filled the follicle except for a cystic space or lacuna formed suprabasally Usually a single follicle was involved The lesion was fairly sharply bounded by what appeared to be the connective tissue sheath of the follicle

Higher power showed striking basal cell hyperplasia and resultant papillomatosis Multiple minute prolongations extended into the basal epithelium from the suprabasal lacuna In some areas the epithelium was arranged in whorls simulating pearls The lacuna was filled with acantholytic and dyskeratotic cells (corps ronds and grains) (Fig 45) The corps ronds contained an eosinophilic, hyalin like cytoplasm and a large centrally placed basophilic nucleus Some had also an eosinophilic body in the cytoplasm which suggested an inclusion

The hypothesis that the lesion is caused by an infectious agent, probably viral seems most tenable though proof is lacking Excision is the treatment of choice, for the lesion tends to recur after irradiation, desiccation and curettage Follow up of 36 patients for an average of 5 3 years yielded no evidence of malignant change nor was there a hereditary background of Darier s disease in any patient On the basis of present knowledge the term isolated dyskeratosis follicularis most aptly describes this entity and is preferable to isolated Darier s disease and other terms that have been used

Keratosis Follicularis Serpiginosa Lutz (Elastoma Intrapapillare Perforans Verruciforme Miescher) Kai Dammert and Tauno Putkonen[6] (Univ of Helsinki) report a case

Boy 16 had had an eruption on the nape of the neck for 6 years The eruption did not itch and was below the hairline There were 20 30 discrete papules and a number of confluent papules forming dense circinate ridges or rings The papules were 2 3 mm in diameter, with redness at the edges and a gray keratotic scale in the center The scale was removed with difficulty leaving a bleeding depression The skin surrounding the lesion was normal except for an area about 3×3 cm to the left of the midline This area appeared atrophic and was partially bordered by ridges and papules The hairs were preserved in this area but the normal skin surface was interrupted by several small low light colored depressions Near the peripheral ridges were parallel low folds

During a year the configuration of the eruption changed slowly

(6) Dermatologica 116 143 155 March 1958

A few new papules appeared and old papules coalesced in places forming new ridges (Fig 46) The shape of the old ridges changed and breaches appeared in them as the process subsided in places The peripheral ridge advanced 2 mm in 1 year

Development of the lesion was studied by serial sections of the keratopapular ridges and the skin adjoining them on both sides The first change was an increase of elastic tissue in the upper dermis Then followed a keratopapular stage characterized by a necrobiotic and necrotic process accompanied by granulomatous and simple chronic inflammatory changes Fibrous healing marked the final stage in the proce s Mo t of the excessive elastic ti sue had disappeared but dense aggregations persisted in some papillae where they formed elevated elastomas

The author conclude that the clinically active keratopap

F g 46 Le on f k rat i f the lat serp gin sa on pe of neck 1 yea f fi t observ t (Court y f D mm rt h a d I tkon T D rmat l gi 116 143 155 M h 1958)

ular stage starts deep at the tips of the rete pegs The exces ive elastic tis ue invades the epidermis causing destruction of the involved ti ue and an inflammatory reaction This view differ somewhat from previou concepts The authors found no follicular changes and could not demonstrate that the hyperplastic and hypertrophic elastic tissue was a result of degeneration Intrapapillary elastomas were seen only in areas of fibrous healing Outside the ridge or in the kerato papular lesions no den e papillary aggregations of elastic ti sue were ob erved and thu such aggregations in them selves *could carcely* be important in the development of the papular inflammatory tage of the disea e The cause of the increased elastic fibers in thi disease is not known How

ever in at least 6 of 7 reported cases onset of the disease occurred at the prepubertal age, between 9 and 12 year and thus hormonal influences may play a part

Are Hyperkeratosis Follicularis in Cutem Penetrans and Elastoma Intrapapillare Perforans Verruciforme Identical? According to Z Zambal[7] (Univ of Zagreb) hyperkeratosis follicularis et parafollicularis in cutem penetrans elastoma intrapapillare perforans verruciforme and keratosis follicu-



Fig 47—Verruciform chang o l ft knee and d rsally from head of fibula (Courtesy of Zambal Z Hautarzt 9 304 311 July 1958)

laris serpiginosa denote the same disease The clinical characteristics are follicular papulonecrotic lesions which may be isolated *circinate serpiginous or grouped (verruciform)* The author s patient a woman *23 showed simultaneously* circinate serpiginous and verruciform (Fig 47) lesion Along with the *follicular changes there were some nonfol*licular lenticular papules and yellowish maculosquamous lesions

The disease process seems *to be basically follicular* The follicular perforation is probably induced by hair and frag-

(7) Hautarzt 9 304 311 July 1958

ments of hair cuticle Without perforation no histologic diagnosis can be made Histologically besides the epidermal changes there are foreign body granulomas with phagocytic fragments and also mycelium like fibers in the follicle (near the place of perforation) The number of elastic fibers within such follicles is usually small In addition to the histologically important changes of the elastic and collagen fibers in the subpapillary layer corresponding to cutis hyperelastica the patient presented all clinical symptoms of the Ehlers Danlos syndrome

It is suggested that the described dermatosis develops in patients with cutis follicularis serpiginosa and that it is essentially a dysembryoplastic disease

Acrokeratosis Verruciformis according to Jeronimo Lopez Gonzalez[8] (Univ of Mendoza) was originally defined by Hopf in 1930 as an entity characterized by hard warts localized exclusively on the hands and feet and appearing during puberty In 1933 Hopf studied 4 cases in which the warts extended to other skin areas The lesions appeared early at birth or in the first years of childhood

Acrokeratosis verruciformis is considered a nevoid disease because of its frequent association with various types of nevi It is familial i e a genodermatosis due to an anomaly of cornification It affects both sexes equally The lesions are papular and vary in size from that of a millet seed to that of a lentil They are polygonal with definite borders and are slightly elevated skin or chestnut colored and single or confluent The lesions resemble verruca plana are of lichenoid appearance and are of hard consistency They are not scaly With the slightest trauma they may give rise to blisters They are usually located on the dorsal surfaces of the hands and feet with mosaic distribution but retain their individual character The intermediate skin may be lichenified On the palms and soles the condition appears similar to punctate keratosis Occasionally other parts of the skin are involved The nails are opaque and fragile and there is some hyperhidrosis and acroasphyxia

Histologic examination of the skin shows considerable hyperkeratosis hypergranulosis and hyperacanthosis with discrete papillomatosis There is no parakeratosis or cellular vacuolation as is observed in verruca plana

[8] A h ten d ma 7 3 9 366 December 1937

The course of the disease is chronic The lesions do not regress spontaneously but they display no degenerative changes Treatment is of little value

Man 22 had a dermatosis which began at age 9 His father had had a profusion of warts since childhood and a sister 9 had begun to show a similar skin picture during the past few months The patient s verrucous lesions at first were localized on the dorsum of the hands and feet but later extended to the legs and forearms and finally to the axillary folds and hairy skin In the outer ear and temporal region



Fig 48 —P pul q mou le ı n f au lar pa l (Co rtesy f G n l z J L. Arch a gent dermat 7 359 366 D mber 195)

there were dirty crusts (removed with the curet) alternating with crabby papules (Fig 48) Flat pinhead sized papules formed irregular plaques in the axillary inguinal and uperior thoracic regions The nails were striated longitudinally The face was covered with an acne and biopsy of a skin lesion from the dorsum of the hand showed hyperkeratosis hypergranulosi and acanthosis with pronounced papillomatosis in the derm Lymphocytic infiltration coincided with zones of epidermal parakeratosi Biopsy of the retroauricular area showed similar hyperker itosi and granulosis Papillomatosis in the dermis was discrete and lymphohistiocytic infiltration was perivascular Pilosebaceous connections were markedly hyperkeratotic The sweat gland showed no changes Dactylo copy revealed interruption of the papillary lines

Pityriasis Rubra Pilaris in Identical Twins aged 10 is reported by Erik A Knudsen[9] (Finsen Inst Copenhagen) The lesions were mild and the disease was diagnosed in 1 child only when the sister was also examined There were no other known cases of skin disease in the family

Leitner reviewed 152 cases of pityriasis rubra pilaris and concluded that the disease is invariably hereditary assuming (as is probably correct) that there exist mild cases which are not recognized Leitner s survey included genealogic tables of 15 families in which 2 or more cases occurred These were analyzed by Ford who concluded that the disease is probably always dominantly inherited it is therefore to be expected in half the offspring of a diseased person and in half the members of an affected family of sisters and brothers Ford however attached particular importance to 3 tables in which the parents of those affected did not have the disease though in other respects the familial tendency was obvious at least in 2 of the cases Ford suggested that this might arise by mutation or if heterogeneous carriers of the disease were themselves normal i e dominance would be incomplete Mutation could be ruled out in 1 case and thus could not account for all cases Besides the disease is so rare that the number of cases approaches the mutation frequency of the population One of Leitner s own cases was not diagnosed until the patient was aged 40 despite frequent medical examinations and objective symptoms Cases occurring in relative may evidently be missed and for this reason the solitary cases may perhaps also be hereditary

Extracellular Cholesterinosis (Kerl Urbach) Variant of Erythema Elevatum Diutinum is discussed by *J J Herzberg*[1] (Univ Skin Clinic Hamburg) Histologic studies of the patient reported on and of 2 others suggested that extracellular cholesterinosis is essentially a variant of erythema elevatum diutinum The lipid infiltration is a secondary development without nosologic significance

Woman 32 had skin disease for 10 years It started with urticaria [illegible] on the extremities and buttocks which disappeared the following year during pregnancy Four years later the disease recurred with permanent red to brownish violet nodes localized mostly on the extensor surface of the extremities At night and in cold weather pain would recur in the node and the joint beneath them

(9) B[illegible] J Dermat 70 7 29 J[illegible]uary 1958
1 Arch kl[illegible] [illegible] Dermat 05 4 49 1 58

Skin changes would come and go leaving behind pigmentations with or without scars Occasionally bloody blisters would appear in the area of the nodes with considerable pain X ray treatment failed

Physical examination was negative except for colpitis simplex and the mucosal and skin changes The latter affected the buttock the area of the Achilles tendon the anthelices and symmetrically the extensor surfaces of the upper arms down to the elbows the knee area extending to the proximal part of the leg and the distal part of the thigh The oral mucosa was also involved The affected areas revealed brown polycyclic and sharply defined elevated efflorescences which varied from pea to larger than thumbnail size and occasionally coalesced to plaques The surface of most lesions was scaly Some were covered with bloody crusts while a few on the extensor surface of the fingers were ulcerated Near these acute foci there were pigmented or depigmented scars and atrophic areas of old foci The buccal mucosa on the left showed a lentil sized, translucent whitish yellow tumor with superficial vascular markings

During a 1 year hospital stay some of the nodes regressed spontaneously with pigmentation and with or without scar formation In attacks erythema exudativum like eruptions appeared on the extensor surface of the forearms and thighs From time to time large painful blood filled blisters developed rather suddenly within the area of the nodes After removal of the blisters a circumscribed necrotic area remained which because of secondary infection healed with scar formation On the buccal mucosa and on the hard palate under the plates erosions and papules were observed

Histologic examination of 3 day old nodes revealed edema of the subepidermal connective tissues The vessels of the superior plexus were surrounded by masses of polymorphonuclear cells situated in loose perivascular connective tissue the latter consisting of broken up collagen fiber These infiltrations contained also histiocytes very few lymphoid cells and rarely an eosinophil cell Macrophages plasma elements and storage cells were absent The capillaries were dilated their endothelium swollen and the lumen filled with a reddish homogeneous mass which was not a thrombus

Examination of older nodes showed fibrin masses in the corneal layer and slight leukocytic infiltration between corneal and granular layers The intercellular fissures in the basal layer were widened a few basal cells showed vacuoles The upper two thirds of the remaining cutis showed an extensive cell rich infiltrate mostly around the heavily damaged vessels consisting of polymorphonuclear leukocytes rare eosinophils histiocytic elements and a few lymphoid cells Within the infiltrate there were many nuclear fragments and in some areas macrophages There were few large cells with foamy plasma No giant cells were observed The number of capillaries was definitely increased their lumen filled but not widened with leukocytes and red blood cells

The structure of the connective tissue was altered Sudan III staining showed a partly diffuse partly focal orange colored extracellular collection of lipid Very few large cells contained reddish brown droplets in the cytoplasm

Of several forms of therapy tried only ACTH by intravenous drip and cortisone influenced the skin eruptions and the joint symptoms favorably

Lipoid Granulomatoses of Subcutis were studied by H Lausecker (Genl Hosp St Polten Austria) Lipoid granulomatosis denotes a morphologic entity occurring in various diseases The Hand Schuller Christian and Abt Letterer Siwe diseases and eosinophil granuloma of the bones are considered as various forms of the same basic disease especially in the Anglo American literature The latter is thought of as an infectious granulomatous disease with remarkably phasic course Diagnosis is based solely on the histologic changes The clinical picture may vary to a great degree depending on the type of the disease and age of the foci

Woman 37 had many lipoid granulomatous nodules appear in the subcutis over 2 years accompanied by enlargement of the liver spleen and lymph nodes X rays showed light osteoporosis Serum cholesterol level were constantly at the upper limit of normal and the ratio of free cholesterol to cholesterol esters was about 1 5 During 4-year follow up the symptoms and signs of the disease disappeared probably independently of the treatment (diet x rays) Thus lipoid granulomatosis proved transitory in this patient Histologically the nodes of the subcutis showed all four phases of lipoid granulomatosis and the round cell infiltrate consisted almost exclusively of plasma cells

Involvement of the lymph nodes spleen and liver suggest that this patient had a generalized disease that also affected the subcutis The author suggests that lipoid granulomatosis is an infectious allergic disease process in patients with an abnormal constitution

Case of Infantile Xanthomatosis is described by Aldo Leoni and Silvio Bressanin[3] (Univ of Padua)

Boy aged 15 months poorly developed had a lesion in the scrotum at birth Several months later papular and nodular lesions appeared on the scalp then on the forehead temples back chest and extremities They were wheat to lentil sized slightly elevated round with clearcut border parenchymatous fawn colored isolated and without inflammation Lipid findings were normal

Histologic study revealed a slightly thinned epidermis with marked flattening of the intercapillary elements and the dermal papillae The malpighian layer was altered and the horny layer slightly thickened The superficial layers of the skin showed intense reticuloendothelial proliferation with foam cells rich in protoplasm and a large nucleus that stained easily with sudan III In the infiltrate were numer

(2) H ut at 9 163-169 April 1958
(3) M m dermat 33 36-239 J 1958

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the hyalinized collagen surrounding these fibers and the particles of calcium were not digested Elastic tissue from normal skin and ligamentum nuchae exposed to elastase showed changes identical with those seen in the biopsy specimen Control collagen fibers were unaltered

Darkfield examination of the microincinerated sections showed heavy deposits of the white ash characteristic of calcium and/or magnesium in the mid and lower dermis In the involved area of the dermis the white ash existed in irregularly dispersed large clumps Occasional rod shaped fibers some sharply angulated were found in and adjacent to the large calcium clumps All these discrete fibers were sharply outlined with the white ash and appeared to contain granules that reflected light in a manner indistinguishable from the large masses

In sections viewed by electron microscopy the appearance of the altered fibers was typical of elastic tissue and did not resemble collagenous tissue These fibers were surrounded by and mixed with fibers with the 640 A periodicity typical of collagen

On the basis of these findings the authors believe that the fibers in pseudoxanthoma elasticum which have an affinity for the established elastic stains and which resemble elastic tissue in hematoxylin and eosin stains are actually elastic fibers These altered elastic fibers may act as foreign material evoking an inflammatory and giant cell reaction calcification and eventually an increase in collagenous fibrous tissue in the involved portions of skin Results of this study do not exclude the possibility that both elastic and collagenous fibers are primarily involved in this disease though this seems much less likely

► [Some authors are of the opinion that the fibrous elements affected in pseudoxanthoma elasticum are collagen fibers Shaffer Copelan and Beer (A M A Arch Dermat 76 622 1957) called attention to the triad of pseudoxanthoma elasticum Paget s disease and angioid streaks and reported a case of pseudoxanthoma elasticum associated with calcinosis of the subcutaneous tissues and widespread calcification of the major blood vessels —Eds]

Idiopathic Atrophoderma of Pasini and Pierini According to Orlando Canizares Jerry M Sachs Leon Jaimovich and Victor M Torres[5] (New York Univ Post Grad Med School and Bellevue Hosp) progressive idiopathic atropho

(5) A M A Arch Derm t 77 4 60 J uary 1958

ous foreign body giant cells and some round empty spaces bordered by a crown of flattened cells thought to be newly formed transected endothelial tubules In the deep layers the sudanophil elements were less numerous with infiltrates of lymphocytes The connective tissue collagen in the lesion had almost disappeared and showed homogenization at the periphery

Because of the absence of hereditary or familial element of involvement in other organs or tissues and of primary systemic processes in the reticuloendothelial system the diagnosis was restricted to the group of disseminated xanthomas of infancy with normal lipid values The authors diagnosis was infantile xanthomatosis although the case was much like nevoxanthoendothelioma Congenital infantile xanthomatosis is rare in Italy this being one of the few cases reported so far

Studies on Nature of Abnormal Fibers in Pseudoxanthoma Elasticum Thomas J Moran and Albert I Lansing[4] (Univ of Pittsburgh) studied involved skin from a typical clinical and histologic example of pseudoxanthoma elasticum by standard histologic methods elastase digestion microincineration and electron microscopy

Histologic examination of hematoxylin eosin stained slides revealed the characteristic changes of pseudoxanthoma elasticum in the mid and lower dermis An irregular but fairly sharply outlined nodular band of altered often hyalinized fibers of bundles was found in whorls or irregular streaks around particles or clumps of blue staining material resembling calcium Sections stained with orcein showed many varying sized fragmented often thick and irregular red fibers which were indistinguishable from elastic tissue elements These were principally in the calcified portion and were surrounded by wide bundles of tissue resembling collagen

Observation of the sections after digestion with elastase showed the characteristic change of elastic tissue The fiber staining red with orcein assumed a prominent transverse elastic segmented striped or ladder appearance as they underwent partial dissolution (15 minutes) After 2 hours almost all these fibers in the elastase covered areas had disappeared though a few thick fibers were still seen These also showed a striped or segmented appearance The involved fibers in areas protected from elastase action were unchanged and

(4) A M A Arch Path 65 (98 (96 June 1958

Differential Diagnosis between Morphea and Idiopathic Atrophoderma of Pasini and Pierini

Morphea	Idiopathic Atrophoderma of Pasini and Pierini
Sex	
More common in women	More common in women
Age at on et	
Mostly between 20 and 50	Teens or early twentie
Location	
Extremities especially lower trunk face and neck	Chiefly trunk back always affected hands feet and face almost in variably free
Duration of activity	
Average 3—5 years	Progres ive 10—20 years
Clinical appearance	
At on et thickened indurated pink or mauve colored patches	At onset soft depressed with cliff drop border blui h brown or bluish violaceous patches No lilac ring
Later center pales becomes ivory colored with peripheral lilac ring unpinchable at tached to deeper structures patches seldom run together	Later patches vary run together forming larger patches large veins faintly visible areas of sclerodermatous changes may appear in center
Course	
May disappear spontaneously without leaving sequelae or *may leave a slightly atrophic* hyperpigmented patch	Usually progressive until reaching a standstill there is no involu tion *of lesions occasionally* concomitant lesions suggesting morphea in edematous stage in volute into soft depressed bluish plaques
Histopathologic characteristics	
Edema of collagen which may ex tend in upper cutis to deeper cutis pronounced sclerosis elastic tissue changes absent or minimal if present appear late	Edema of collagen in mid and deep cutis no sclerosis elastic tis sue changes concomitant with edema in deep cutis deep ves sels engorged in patches pre senting pronounced edema of collagen simultaneously with elastic tissue changes when the former subsides the latter re mains

cially the back The face hands and feet are almost invari ably free (3) Individual lesions vary from a few centimeters in diameter to large patches (4) The lesions are bluish vio laceous or brownish blue and are depressed from the sur rounding skin (Fig 49) with a sharp abrupt cliff drop border or a gradual slant (5) There is faint blurred visibility of the deeper blood vessels (6) The surface of the lesions is smooth and normal except for color (7) No induration is palpable (8) The skin around the patches is normal (9) If

derma of Pasini has not received attention as such in the American dermatologic literature During the past 20 years Pierini has observed over 50 cases and has made invaluable contributions to the knowledge of this condition For this reason the authors suggest the term idiopathic atrophoderma of Pasini and Pierini for this peculiar cutaneous atrophy

They present 5 cases 2 in males and 3 in females Onset

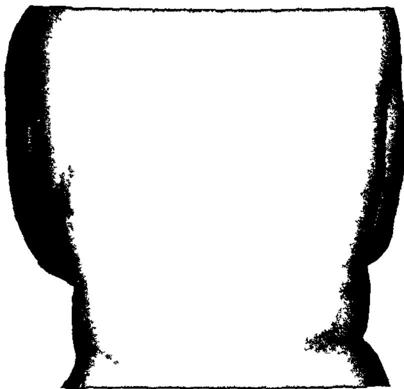


Fig 49—Multiple depressed patches on back of patient Two show cle odermatous changes (Courtesy of Canizares O et al A M A Arch Dermat 77 4 40 January 1958)

was in the teens or early twenties The lesions were on the trunk always affecting the back In 4 cases the lesions were asymptomatic 1 patient had occasional tingling or sensation of warmth The slow progressive course ranged from 4 to 15 years Although no complete involution was observed there was an apparent spontaneous arrest in 2 case

The clinical characteristics of idiopathic atrophoderma of Pasini and Pierini include the following (1) Onset is in the teens or twenties (2) The trunk is chiefly affected espe

preparations and cultures from the inguinal lesion were negative Biopsy of a neck lesion showed familial benign chronic pemphigus

Of the 6 patients 2 had familial history of the disease Four had exacerbations in hot weather Although this disease is considered rare in the Negro 4 of the patients were Negroes Systemic administration of antibiotics was beneficial in 5 of the patients

► [One must be constantly alert for the atypical features of this disease because sometimes the diagnosis will hinge on their recognition Fortunately the biopsy is usually diagnostic —Eds]

Problems and Results of X ray Examination of Skin and Its Diseases II X ray Findings in Pathologically Changed Skin are discussed by Gotthard Lemke[7] (Univ Skin Clinic Freiburg) In diagnostic x ray studies of the skin the subcutaneous fat tissues serve as physiologic contrast mediums The fine structure of the normal skin can be visualized by soft x rays if its components are of macroscopic size The skin changes in various dermatoses can be demonstrated by x rays because of differences in volume absorption and density Skin diseases not accompanied by these differences cannot be visualized by x rays

X ray pictures present only the conditions at a given moment Serial follow up films however indicate the changes taking place over a period of time Serial films reveal not only gross skin change but also transient or clinically insignificant symptoms such as wheals in urticaria

In several skin diseases a characteristic and often pathognomonic x ray picture is observed which allows a diagnosis without knowing the clinical or other data In certain instances x rays reveal changes which are not suspected by routine clinical studies Thus the wheals in acute and also in chronic relapsing urticaria are represented in the x rays by changes in the reticular network of the subcutis besides the clinically suspected broadening of the cutis line This is observed regularly and independently of the size and age of the wheal In older larger wheals it is even possible to demonstrate muscular involvement in the form of ill defined and loosened muscular fascia This would suggest that not only the capillaries and the smallest vessels of the cutis are involved but also those in the adjacent layers of the subcutis Similarly changes can be detected regularly in the subcutaneous fine structure in erythema exudativum and in psoriasis

(7) Arch f Dermat u Syph 207 5 6-616 19 9

sclerodermatous changes appear they develop years later within the patches of atrophy (Fig 49) or simultaneously in separate lesions In some cases lesions with clinical appearance of morphea have gradually developed this atrophic picture

The significant microscopic features of the cases cited were edema of the collagen bundles of the deep cutis and accompanying irregular clumping and loss of elastic tissue in this area The fat and epidermis were uninvolved

Although the lesions in *idiopathic atrophoderma* of Pasini and Pierini may show morphea-like features they are not believed to be the disease entity morphea or scleroderma Chief points of differential diagnosis are shown in the table

► [Atrophic lichen planus must be considered in differential diagnosis Here the atrophy may be sharply defined with a "cliff drop" border and some pigmentation may remain —Eds]

Atypical Features in Familial Benign Chronic Pemphigus were observed by Thomas W Lyles John M Knox and J B Richardson[6] (Baylor Univ) in 6 patients

CASE 1 —Man 55 Negro had hyperkeratotic verrucous lesions on the lower legs The neck axillae popliteal fossae groin and sacral area showed scattered vesicles surrounded by whitish macerated papules and crusts Biopsies from the axilla groin and a verrucous leg lesion revealed the typical intraepidermal bullae of familial benign chronic pemphigus

CASE 2 —Woman 22 Negro had white-topped papular lesions on the external genitalia which apparently had been precipitated by pregnancy Biopsy showed familial benign chronic pemphigus The eruption disappeared after elimination of leukorrhea that occurred postpartum

CASE 3 —Woman 76 Negro had pemphigoid vesicopustular lesions involving the frontal and preauricular hairline in addition to biopsy-confirmed lesions of familial benign chronic pemphigus in the axilla It was theorized that a pyoderma predisposed to development of lesions in such an uncommon site but it was not possible to determine whether the pyoderma was primary or secondary

CASE 4 —Woman 55 Negro had widespread lesions involving the neck antecubital fossae axillae and thighs The distribution and clinical appearance suggested neurodermatitis disseminata but biopsy showed familial benign chronic pemphigus

CASE 5 —Man 42 white had lesions with erythematous vesicular borders and clearing centers resembling tinea corporis Biopsy showed familial benign chronic pemphigus

CASE 6 —Man 51 white had annular erythematous scaly papulovesicular lesions on the neck and shoulders and a lesion in the groin suggesting monilial intertrigo Repeated potassium hydroxide

(6) A M A Arch Dermat 8 446-453 Octobe 1955

In the erythema nodosum group the cutis is distinctly thickened roentgenographically in the area of the lesion Its lower border is indistinct and the cutis passes gradually into a network of fairly coarse fibers Small meshes are bound by coarse threadlike septa Peripherally and toward the deep layers the lesion merges successively into normal tissue with sparse and slender septa The lower margin of the cutis and its transition into septa resembles a fringed edge of a piece of cloth or the surface of a coar e blanket The clearly visible septa probably correspond to the histologically changed connective tissue areas including the vessels Small areas of fatty tissue observable between them are fairly regular in size and shape

In the erythema induratum group the thickened cutis at the site of the lesion shows a distinct well discernible line of eparation from the subcutis Histologically the septa are slender and less marked and therefore do not appear as distinct as the septa in the erythema nodosum group The subcutis appears diffu ely increa ed in density as in edema with infiltration Connective tissue of regular appearance can no longer be seen marked dense bands without regularity are occasionally observed and these possibly correspond to the course of the subcutaneous vessels

► [It is certainly of interest that the authors are able to discern so much soft tissue detail from x ray studies of cutaneous and subcutaneous tissues —Eds]

Rosacea Like Tuberculid of Lewandowsky W G van Ketel[9] (Univ of Amsterdam) studied 55 patients with rosacea papulosa and papulopustulosa (rosacea like tuberculid) All had thorough physical examinations and one or more biopsies In 37 cases rosacea existed without peculiar clinical or histologic characteristics and without an active tuberculous focus or a clear history of tuberculous infection The Mantoux test at 1 1000 was po itive in 19 of the e ca es and negative in 17

In 6 patients the diagno is of rosacea like tuberculid was con idered on clinical grounds (lateral distribution on the cheeks and neck and/or results of diascopic inspection) In 2 of the e the localization shifted from lateral to medial in the cour e of the di ea e and diascopy became negative In 1 patient two different type of papules were found one

(9) Dermatologica 116 201 10 March 1958

vulgaris These changes are not seen on clinical or histologic examination

All forms of cutaneous subcutaneous tuberculosis studied show common x ray features In the individual case usually a certain sign is in the foreground which is of diagnostic help X rays also reveal the quick clearing of deep infiltrations

X rays may assist in assessment of the pathogenic role of vessels Besides perivascular infiltrations, changes in the vessel wall can also be demonstrated In erythema nodosum the phlebitic and periphlebitic infiltrations appear as poorly circumscribed broadened vascular shadows Thickened vessel walls are demonstrated in necrobiosis lipoidica panarteritis nodosa and circumscribed and progressive scleroderma In periarteritis nodosa vascular changes can be shown by x rays even before appearance of clinical symptoms

Roentgenographic Studies of Cutaneous and Subcutaneous Infiltrates in *Erythema Induratum* and *Erythema Nodosum* are reported by C G Leczinsky and O Mattsson[8] (Karolinska Hosp Stockholm)

METHOD—The skin eruptions were recorded with a tangential beam To achieve this an indicator was applied to the center of the affected skin surface The central beam could be easily adjusted in relation to the efflorescence under fluoroscopic control with the image intensifier by means of a special variable diaphragm the irradiated field could be reduced selectively to a minimum Thus the amount of secondary radiation and the so called extrafocal radiation were also reduced with resultant improvement in the quality of the image Recordings were made on a nonscreen film using 40 50 kv

Twenty cases of panniculitis of the lower legs were studied Typical x ray appearances were found in two main types of subcutaneous changes which the authors call the erythema nodosum and erythema induratum groups Included in the former group were typical cases of erythema nodosum, some cutaneous forms of periarteritis nodosa and erythema nodosum migrans and perstans The erythema induratum group consisted of tuberculous and nontuberculous erythema induratum Darier s subcutaneous sarcoid Weber Christian disease in certain stages and several similar affections Besides the erythema induratum and nodosum groups an intermediary group was also seen Of the 20 cases 7 were erythema nodosum in type 9 induratum and 4 intermediary

(8) Acta radiol 49 193 204 March 1958

f ction decreased during the 6 years of the study Whereas in 1951 53 73% of 49 children were tuberculin positive in 1954 56 this proportion fell to 51% of 56 cases Of the 65 children with positive tuberculin tests 46 had clinical and radiologic evidence of a recent and active tuberculous process and in 19 the only evidence of the tuberculous infection wa the positive kin te t The proportion of children having active primary tuberculosis was 55% in the first 3 years and 34% in th e ond period Of the 46 children with active primary tuberculosi 10 had important tuberculous complication within 9 months of the appearance of erythema nodosum tuberculou meningitis in 3 bronchopneumonia in 1 arthritis of the hip in 1 pleural effusion in 3 and pustular conjunctivitis in 2

Five children exhibited erythema nodosum after BCG vaccination and in 4 of these the eruption occurred at the time of tuberculin conversion Nevertheless in 3 of the children there was al o evidence of streptococcic infection at the time the eruption appeared

Of 35 patients whose tuberculin te ts and radiographs were negative at the time of erythema nodosum 17 had a sore throat within 2 weeks before the eruption In 10 of these laboratory evidence of a beta hemolytic streptococcic infection wa obtained In 19 children no investigations were performed to prove a possible streptococcic etiology In most of the tuberculou patients no further investigations were carried out after evidence of tuberculosis was found However erythema nodosum was preceded by sore throat in 15 and streptococcic infection was demonstrated in 5

The e findings indicate that tuberculosis is still an important etiologic factor in erythema nodosum in children but its importance is steadily decreasing As BCG vaccinations are increasing in number it will have to be considered as a pos ible cause in cases of erythema nodosum The true incidence of streptococcic etiology will not be known until all ca es are investigated routinely by throat swabs and estimation of anti treptolysin titers When this is done many cases of erythema nodo um will probably be found in which multiple factors operate

showing no reaction to diascopy and the other showing a reaction Changes in localization and in diascopy occurring in the course of the disease prove that clinical differentiation between rosacea and rosacea like tuberculid is impossible In half the patients with clinical findings suggestive of rosacea like tuberculid no evidence of a tuberculoid structure was found in microscopic sections of the papules Of 49 clinically normal rosacea patients, 5 showed a clear tuberculoid structure and 4 showed signs of such structure Thus tuberculoid structures are not rare in rosacea papulosa and histology cannot be conclusive in differentiating rosacea and rosacea like tuberculid

No connection was found between the presence of tuberculoid infiltrates and the results of examination for tuberculosis However 3 patients with clinically normal rosacea and no evidence of tuberculoid structure histologically had an active tuberculous focus or a definite history of such infection Since rosacea may be present with tuberculous lesions in other parts of the body examination for tuberculosis is of little value in differentiating between rosacea and rosacea like tuberculid

Neither clinical nor histologic examination separately or combined constitutes an effective criterion for distinguishing rosacea from so called rosacea like tuberculid Rosacea like tuberculid of Lewandowsky is not to be regarded as a separate disease and must be considered identical with rosacea papulosa or rosacea papulopustulosa

► [There are reasons for abandoning the term rosacea like tuberculid of Lewandowsky e g those first pointed out by Snapp who suggested the name Lewandowsky s rosacea like *eruption* and now those given by van Ketel There is a very small group of cases which clearly show apple jelly nodules clinically and tuberculoid structures histologically and which also have some features of rosacea. These cases should be considered lupus miliaris disseminatus faciei or micropapular tuberculid. The remainder should be classified with rosacea or acneiform eruption or whatever other entity they fit in best —Eds]

Changing Etiology of Erythema Nodosum in Children

Among 105 consecutive children with erythema nodosum seen during 1951 56 John Lorber[1] (Children s Hosp Sheffield England) found a positive tuberculin test as a result of natural infection in 65 (62%) Incidence of tuberculous in

(1) Arch Dis Childhood 33 137 141 Apr 1 1958

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(1) Arch Dis Childhood 33 137 141 April 1958

C wernecki into the palm soles and glabrous skin of 2 human volunteers were un ucces ful

► [Here is another of the few pigmented le ions of the palms other than nevi that should be considered in differential d agnosis —Eds]

Extensive Trichophyton Infections of about 50 Years Duration in Two Sisters are reported by F Blank P Schopflocher I Poirier and J L Riopelle[3] (McGill Univ) The eruptions were widely distributed over the body and resulted in alopecia totalis in both patients Many deep granu



Fig 5 G l m t l on b k (Cou t y f Bla k F et al D rmato-l g 115 40 51 J ly 1957)

lomatous lesions were present in 1 case only (Fig 50) It is difficult to explain why the dermatophyte invaded the dermis of 1 ister and under apparently similar conditions restricted its pathogenic activitie to the epidermis in the other Special yet unknown conditions must prevail so that the fungus a highly specialized parasite of the keratinized layers of skin nail and hair becomes capable of living and multiplying in the dermis These special conditions apparently are rarely met since dermatophytosis is common but inva ion of the dermis is rarely reported

(3) Derm t log ca 115 40-51 J ly 1957

II FUNGOUS INFECTIONS

Tinea Nigra Palmaris Disorder Easily Confused with Junction Nevus of Palm is described by J Graham Smith Jr Wiley M Sams and Frank J Roth Jr[*] (Univ of Miami) *Tinea nigra palmaris* is caused by the fungus Cladosporium wernecki In the western hemisphere nearly all reported cases have involved the palms however cases involving other areas of the body such as the neck or thorax do occur The asymptomatic macular lesions neither elevated nor scaly are brown or black appearing as an India ink or silver nitrate stain The disease must be differentiated from nevi contact dermatitis pigmentation of Addison s disease and drug eruptions The disorder responds readily to local therapy with keratolytic agents such as salicylic and benzoic acids The authors report 2 cases Both were mistakenly diagnosed as nevi 1 by experienced plastic surgeons and the other by competent dermatologists

CASE 1—Woman 55 who had not been out of Dade County Fla for 10 years had an asymptomatic brown macular lesion on the left palm It gradually enlarged during 2½ months It was not elevated or scaly and measured 2×2 cm Microscopic examination of a scraping in 10% potassium hydroxide revealed branching hyphae Cultures were identified as C wernecki The patient was treated with 3% salicylic acid ointment The lesion completely disappeared except for residual erythema in 3 weeks

CASE 2—Physician s daughter 5 had a small asymptomatic 6×10 mm pigmented lesion on the right palm The lesion looked like cafe au lait pigmentation and was of normal texture No mycologic examination was made and the lesion was excised with a preoperative diagnosis of pigmented nevus Microscopic examination revealed hyphae and spores in the upper stratum corneum and a minimal perivascular infiltrate of lymphocytes and histiocytes in the upper dermis The pathologic picture was considered diagnostic of tinea nigra

Including these a total of 3 cases of tinea nigra palmaris acquired in Florida and 4 from Texas have now been reported in the United States Case 1 is the first reported in the United States in a patient over age 12 Attempts at experimental reproduction of the disease by inoculation of infected scales from the first patient and material from a culture of

(*) J A M A 167 312 314 May 17 1958

in 9.4% of abnormal asymptomatic interspaces and in 64.7% of those with symptoms. The association of coagulase positive staphylococci with the presence of symptoms was statistically significant. There was no significant variation in the distribution of other bacteria in either the 1st or 4th interspace of patients with normal interspaces, asymptomatic abnormal interspaces and symptomatic interspaces.

Recovery of both pathogenic fungi and staphylococci from the same interdigital space occurred in 11.4% of subjects. Though this association was found in only 2.2% of normal interspaces and 3.1% of those without symptoms, it occurred in 47% of those with symptoms. This finding was also statistically significant. A pathogenic fungus was found with a beta hemolytic streptococcus in 1 person with abnormal skin but no symptoms and in 1 with symptoms.

The results suggest that clinical symptoms of tinea pedis are the outcome of the association of pathogenic fungi and staphylococci even in cases without acute inflammation and which are usually regarded as purely mycotic in origin. If this is so, some alteration in treatment of athlete's foot might be worth considering. In subjects with extensive secondary infection of the foot, a preliminary course of mild treatment to reduce inflammation before the application of fungicides is usually advised. It is possible that a two-stage treatment in all forms of athlete's foot with subjective symptoms, the first stage directed specifically toward the staphylococcus and the second toward the fungus, might produce a more satisfactory result.

► [This study reveals that just as pathogenic fungi can often be found in clinically "normal" feet, so can coagulase positive staphylococci also be recovered. The question, of course, is whether the staphylococci contribute to the activity of the fungi to produce clinically discernible changes or whether the staphylococci merely grow in the suitable terrain prepared by the fungi. We would suspect the latter explanation to be correct, as appropriate antifungal therapy alone is usually adequate to care for the infection. The availability of antifungal antibiotics, such as griseofulvin, which is effective on oral administration, may help to answer this as well as many other hitherto unanswerable questions in the field of superficial fungous infections.—Ed.]

Fungous Disease as Complication of Steroid Therapy is discussed by Robert F. Burns[43] (Henry Ford Hosp.). There is general agreement that systemic steroids promote dissemination of deep *fungous* infections in laboratory animals. However, this observation cannot necessarily be applied to

[43] A.M.A. Arch. Dermat. 77:686-689, June, 1958.

A biopsy specimen from the patient with granulomatous lesions showed granulomatous reactions within the entire cutis Short and long septate hyphae were found in large multinucleated giant cells and interstitially Hyphae could not be demonstrated in small foci of necrobiosis No keratinous material could be detected in any section The fungus may have penetrated through the hair follicle into the dermis After it had digested all the keratinous material present the dermatophyte became adapted to the changed ecologic conditions i e to living without keratin in the dermis

Trichophyton epilans was isolated in both case The cultures isolated from the deep granulomatous lesions varied slightly in some colonial and microscopic features from those isolated from scaly eczematous lesions in the same patient and in her sister The authors do not believe that two species were involved but that the alteration in the fungu morphology was the result of adaptation to a keratin free environment

Oral administration of potassium iodide and x ray treatment caused remarkable regression of the granulomatous lesions in the first patient

► [It would have been interesting to know whether any abnormality in the anatomy or physiology of the skin was present in these 2 sisters and whether there was any family history of such abnormalities This might have explained the coincidence of a persistent and extensive fungous infection in both sisters as it did in the patient with widespread T rubrum infection studied by Baer and Muskatblit (Arch Dermat & Syph 56 834 1947) —Eds]

Search for Presence of Pathogenic Bacteria and Fungi in Interdigital Spaces of Foot of 175 subjects was carried out by Mary J Marples and Margaret J Bailey[4] (Univ of Otago) In 45 the interdigital spaces showed no abnormality clinically though 13 had had athlete s foot previously In 96 there was asymptomatic maceration or scaling in the 4th interdigital space or in other spaces besides the 4th In 34 subjective symptoms were present and one or more interdigital spaces showed maceration scaling or fissuring

Pathogenic fungi were demonstrated in 20% of all subjects Fungi were present in 8 9% of those with normal interdigital spaces in 12 5% of those with asymptomatic abnormal spaces and in 58 8% of those with symptoms Coagulase positive staphylococci were isolated from 20% of the subjects They were found in 8 9% of normal interspaces

(4) Brit J Dermat 69 379 388 November 1957

that such treatment produce a tendency to development or to flare ups of superficial fungous infections —Eds]

Comparative Studies of Special Mediums for Identifying Candida Albicans from Other Candidas and Molds Many laboratory procedures have been proposed but the most simple rapid and inexpensive technic for identifying C albicans is to demonstrate chlamydospore formation This diagnostic spore formation can be induced on corn meal rice infusion and bactochlamydospore agars A culture medium proposed by Nickerson contains as an active ingredient a complex polybismuth sulfite

Bahram Sina and Frederick Reiss[6] (New York Univ Post Grad Med School) used a known strain of C albicans and 30 strains of candida species freshly isolated from lesions of the skin and mucous membranes in a comparative study of these culture mediums The known strain of C albicans grown on rice agar formed chlamydospores in 5 days whereas it required 10 days on corn meal agar and bacto chlamydospore agar None of the strains of C krusei C parakrusei C guilliermondi C stellatoidea C tropicalis and C pseudotropicalis which were grown on these mediums produced chlamydospores Candida albicans occasionally produced chlamydospores as early as the 2d day of incubation on rice agar but not on the other mediums Of the 30 strains of C albicans all produced chlamydospores on rice agar 23 on corn meal agar and only 20 on bactochlamydospore agar

Nickerson s agar is not recommended as a routine procedure for identification of C albicans since a number of species not belonging to genus Candida are also capable of reducing bismuth and forming jet black or brown colonies Rice infusion agar is most suitable for identification of C albicans

Rapid Serologic Differentiation of Candida Albicans from Candida Stellatoidea The commonly accepted criterion for routine identification of C albicans in culture is the production of chlamydospores on special mediums Though satisfactory for most purposes identification by means of chlamydospore agars is inexact since strains of C stellatoidea a

(6) J I t D rm t 29 263 67 Octobe 1957

man not only because of the difference in response between species but because the steroid dosage in animal experiments is often far in excess of that used in clinical medicine

Clinically there is good evidence that there has been some increase in secondary systemic fungous disease in the past 10 years or so That steroids are the sole cau e of the in crease need not follow In the same decade broad spectrum antibiotics and the cytotoxic agents have come into wide use Few of the recorded cases in which systemic fungous disease followed steroid therapy were of purely cutaneous disease In the main patients had blood dyscrasias lym phomas cancers diabetes widespread burns and similar dis eases with profound systemic implications which would be expected to influence the immune mechanisms unfavorably Besides the patients received not only steroids but antibiot ics or cytotoxic agents or both

Increase in mortality from secondary fungous infections lies chiefly in systemic moniliasis, aspergillosis and hi to plasmosis with some increase in mucormycosis and crypto coccosis Coccidioidomycosis and blastomycosis are not con sidered to have increased in frequency with steroid admin istration There is also considerable evidence that large doses of steroids may have a virulence enhancin effect on human superficial mycoses

An awareness of the risk of dissemination of fungou di ease by steroid therapy is necessary but the danger is not so great that essential treatment should be withheld Good medical precepts should be followed and a complete exami nation, including chest x ray should be performed before major steroid therapy is initiated If this is done and fol low up examinations are reasonably thorough there i little chance of serious trouble Despite these precaution sys temic fungous disease will develop on rare occ ion and this must be counted as a calculated risk of steroid therapy

Superficial mycotic infection should always be brought un der control before the start of treatment if feasible if not active treatment should be carried on during sy temic te roid therapy

► [In our extensive experience with long term s temic and topical corticosteroid therapy during the pa t 8 year we have seen no evidence

that such treatment produces a tendency to development or to flare ups of superficial fungous infections —Ed]

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(6) J I est. Derm t 9 63 67 O t be 1957

saprophyte share with C albicans the ability to form the e spore Morris A Gordon[7] (Med College of South Carolina) describes a simple staining procedure for differentiation of these organisms Fluorescein labeled specific antiserum is applied to smears from culture or clinical material which are then examined by ultraviolet microscopy for fluorescent yeast cells

Although a definitive evaluation of the fluorescent antibody technic as a routine tool for differentiation of C albicans from C stellatoidea must be preceded by work with many more strains of the organisms the method is expected to show about the same specificity and perhaps greater sensitivity than the precipitin test described by Trimble The fluorescent method has the advantages of extreme rapidity and simplicity and can be applied to small number of cell — even a single cell viable or not in pure or mixed culture The technic is also applicable to identification and differentiation of yeast cells directly in smears from suspected mycotic lesions e g those of the vagina In vitro C albicans is readily differentiable from the components of the mixed normal vaginal flora with the exception of C tropicalis This cross reaction may possibly be eliminated by further serologic studies In preliminary work with clinical specimens C albicans has been shown to stain intensely with the appropriate conjugate in oral mucosal smears from cases of thrush

Atypical Favus of Scalp Report of Two Patients with Seborrheic Form is presented by Oscar I Heim[8] (Philadelphia) The distinction between typical and atypical favus of the scalp according to Sabouraud depends on the presence or absence of scutula but in many incidences miliary or minute scutula are found in the atypical forms One of the author's patients was a white soldier 19 who represented a sporadic case of favus from western Arkansas The other was a white soldier 22 who contracted the disease in a known endemic area in eastern Kentucky Both patients had areas of partial alopecia in the scalp covered with layers of grayish white scales (Fig 51) After removal of the scales and after thorough search miliary scutula were found Each scutulum was round about 3 mm in diameter pierced in its center by a parasitized hair and with no concavity of it ... n

(7) J Invest Derm ... 31 1 3 1 5 August 1958
(8) A M A Arch Dermat ... 6 40 51 December 195

perior surface The color was pale yellow which changed to a golden yellow with a drop of 70% alcohol Affected hairs were dull greenish and fluorescent under Wood light Potassium hydroxide preparations and culture revealed Trichophyton (Achorion) schoenleini

The seborrheic form of favus is not easily recognized unless it is kept in mind but if the scalps of all patients who



Fig 1—Large plaque of partial alopecia ... of scalp ... scutula ... away ... (Courtesy ... 6 740 1 December 1957)

present clinical signs of seborrhea sicca seborrheic dermatitis psoriasis and tinea amiantacea are examined for minute scutula and a Wood light is used to detect fluorescent hairs fewer mistakes will be made in diagnosis Both of these patients were seen over a period of years by a number of physicians before a diagnosis of favus was established

In man favus of the scalp irrespective of the clinical form is caused by T (Achorion) schoenleini Though favus located elsewhere on the body may be caused by this fungus such favus can occasionally be due to other dermatophytes

Favus is not considered highly contagious in countries in which hygienic standards are reasonably high but epidemics may occasionally occur in hospitals and schools. Total epilation with x rays is indicated in treating favus of the scalp. Preliminary treatment directed to destruction of scutula is important and close surveillance of the scalp after epilation is necessary to prevent recrudescence.

Comparative Studies on Technic of Fungus Demonstration in Skin and Nail Mycoses With Special Reference to Staining with Parker Ink K. Enderlin[9] screened 134 employees of the public baths in Zurich for fungous diseases of hand, foot and nail. Fungi were sought in the same specimen by culture and microscopically with the standard method and with a new technic using potassium hydroxide and Parker ink.

METHOD.—The specimen (scale, nail fragments, hair) is placed on a slide, covered with a cover glass and impregnated with a mixture consisting of 1 part blue black or blue Parker ink (blue black Parker ink 51 Superchrome) and 9 parts 5-10% potassium hydroxide (nail require the higher concentration). The slide is then placed into a humid chamber for 24 hours. Microscopic studies, even under low power, reveal the blue stained fungous filament.

The Parker ink method was the most successful in detecting fungous filaments. It also revealed interesting details of the growth and behavior of the fungi within the skin. It could be shown how the filaments grew through the cell, how they discharged their spores and degenerated.

Mosaic fungi were found in 44 of the 134 persons. The Parker ink method stained these the same as other fungi. No relation could be found between the incidence of fungous infection and that of mosaic fungi.

From the epidemiologic viewpoint, it was established that washing with soap has no important influence on the growth of fungi, although thorough drying of the interdigital space stops their growth. With marked sweating of the feet, the incidence of fungi seemed to decrease.

► [In the mycology laboratory at the New York Skin and Cancer Unit the Parker ink method was found preferable to the usual potassium hydroxide preparations only with scrapings from micro porum furfur infection.—Eds.]

Sterilization of Pathogenic Fungi by Ultraviolet According to J. Coudert and J. Rondelet[1] (Lyon, France), sterilization of instruments used in beauty parlors, required by public

(9) Dermatologica 116: 34-43, Apr.-May 1958.
(1) Ann. dermat. et syph. 85: 41-419, July-Aug. 1958.

health authorities is fraught with difficulties in practical application. Apparatus for this purpose varies in construction and performance. The authors used a suitable ultraviolet source to test the effect on various types of yeast or fungi often found on the skin and capable of transmission by combs and other instruments used in hairdressing. Despite the favorable circumstances of these experimental tests, resistance of fungous spores to ultraviolet was greater than that of bacteria; dermatophytes in culture were even more resistant.

Pathogenic fungi may be classified in three groups according to their sensitivity to ultraviolet rays: (1) destroyed by irradiation of 1-3 minutes (Candida albicans, Cryptococcus neoformans, Geotrichum candidum, Rhinocladium schenckii beurmanni); (2) sensitive spores but resistant colonies (Trichophyton schoenleini, Ctenomyces mentagrophytes, Sabouraudites canis, Sabouraudites audouini) and (3) spores very resistant to ultraviolet (Rhizopus nigricans, Aspergillus niger). In group 2, spores are sterilized by irradiation for 5 minutes but colonies are not destroyed; they are merely retarded in growth. Irradiation of 40 minutes does not completely destroy S. canis. In group 3, spores of R. nigricans in a thin layer were sterilized in 15 minutes, whereas A. niger was the most resistant organism; spores in a thin smear were sterilized after 1 hour but those in clumps were not.

In contrast, Staphylococcus aureus is sterilized in 30 seconds with an ultraviolet dose of 600 ergs/sq. mm./second. The dosage applied to A. niger was 75,690 ergs/sq. mm./second.

Instruments of complex structure, such as clippers and combs, are not sterilizable by the ultraviolet apparatus currently used, particularly with regard to pathogenic fungi of the skin and hair.

In Vitro Invasion of Hair by Dermatophytes was successfully achieved by F. Kaubitschek (Hebrew Univ.).

METHOD.—Thoroughly washed tufts of hair from 4 healthy girls were incubated with a recently isolated granular strain of Trichophyton mentagrophytes on a rotary shaker for 46 days at 28 C. In 1 girl's hair, several thick hyphae were found invading the substance of the hair running parallel to the long axis. In several places the strands of hyphae formed packets of rectangular arthrospores re-

( ) J. Invest. Dermat. 9:161-164, September, 19

sembling the picture presented by endothrix invasion in naturally occurring tinea capitis

No invasion of hair resembling that occurring in nature has been produced experimentally heretofore The fact that invasion occurred in only 1 of 4 hair samples raises the question whether some hair is resistant to infection in vitro and whether the mechanism is similar to the natural resistance to tinea capitis infections found clinically

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12 BACTERIAL VIRUS PARASITIC AND OTHER INFECTIONS

Unusual Micrococcic Cutaneous Reactions Review of Some Basic Tenets of Micrococcic Bacteriology and Drug Resistance and Presentation of Two Cases The problem of antibiotic resistant micrococci is ubiquitous in contemporary medicine According to Milton Orkin[3] (Univ of Minnesota Hosps) there are two possible mechanisms of penicillin resistance The first involves a micrococcic adaptive enzyme system in which penicillinase is produced in the presence of the specific substrate penicillin This has not been entirely confirmed in vitro but has been suggested as a working hypothesis in vivo If this were the sole mechanism of penicillin resistant micrococci it would seem feasible to withdraw penicillin temporarily from the armamentarium Later reinstatement of the drug might predicate renewed sensitivity via the process of deadaption at least until the production of new adaptive systems

A second mechanism entails the selection of a few resistant mutants *from a large micrococcic population* as a result of destruction by antibiotics of the preponderant susceptible strains This is thought to be a likelier explanation of micrococcic penicillin resistance Selection permits survival and multiplication of the resistant strains with subsequent cross infection to others with a strain which is antibiotic resistant

Penicillin resistance entails multiple steps with gradual development of resistance over months to years In contrast micrococcic resistance to streptomycin isoniazid and aminosalicylic acid develops in one rapid step Highly resistant

(3) A M A Arch Derm t 8 3 8 385 Sept mbe 1958

organisms u ually po e s more genetic variability There fore if the mechanism of selection is accepted the tempo rary removal of a given antibiotic might permit renewed sensitivity on later rein tatement via the process of genetic variability

Production of di ea e by micrococci i attributed to their ability to multiply and spread in ti sues and to their produc tion of extracellular substance including exotoxin leuko cidin enterotoxin coagulase hyaluronidase staphylokina e proteina e and lipases Culture alone i not helpful in sep arating micrococcic secondary infection from colonization since micrococci frequently contaminate broken kin The reaction of the ho t to infectious disea e produces the mani festations of that disease Therefore secondary infection is likely pre ent if many bacteria and polymorphonuclear leu kocytes are present and especially when the leukocytes have phagocytized the bacteria

The problem of antibiotic resistant micrococci is most acute in hospital population Micrococci are well adapted for cro infection in hospitals for the dried organi ms may remain viable and virulent for months or years in dust bed ding mattre se or other fomites Micrococci may thrive for long period in the na al passages of ho pital patient and per onnel

Two case of unusual micrococcic cutaneou reaction are presented The first patient a nur e had cellulitis of the hand due to staphylococci re i tant to erythromycin and sensitive to oxytetracycline and chloramphenicol The second patient had a generali ed pu tular eruption due to coagula e po itive taphylococci which was highly sen itive to penicillin tetra cycline and erythromycin Treatment with penicillin and streptomycin was rapidly effective but there was a recur rence 3 weeks later Culture then revealed staphylococci sen itive to novobiocin and resistant to penicillin and tetracy cline

For diagnosis of an unu ual micrococcic infection a com plete hi tory and laboratory study is nece sary to di tinguish between conditions that may cause similar or identical clin ical pattern Rapid response to specific therapy indicated by bacterial antibiotic sensitivity studies is of diagnostic value Predispo ing condition must be sought as in monilia is *Diabetes* was pre ent in both patients described and a pan

creatic carcinoma in the second The cutaneous infection will probably not be permanently cured until the underlying cause is controlled or eradicated

► [The development of antibiotic resistant strains of staphylococci has produced a major problem especially in hospitals and various approaches to this problem are now being tried In addition to hygienic preventive measures these include the development of new antibiotics and chemotherapeutic agents which are effective against the resistant strains and the enforced withholding of selected antibiotics for certain periods after which they may be administered with the hope that the staphylococci have remained susceptible to them—Eds]

Bacterial Variations in Nasopharynx and Skin of Isolated Arctic Scientists are reported by *Robert W Christie*[4] (Nat'l Inst of Health) Cultures of the nasopharynx and skin of 7 members of an expedition isolated on the Greenland Icecap for 100 days were made at the beginning of the trip and just before they returned

Staphylococcus albus was present in the nasopharynx of 6 subjects initially and in all but 1 of these at the second culturing Staphylococcus aureus was present in 3 initially and in 1 of them subsequently Diphtheroids persisted in 4 of the 5 in whom they were initially present Streptococcus viridans was present in 2 subjects initially and disappeared from both One of these subjects received tetracycline for a severe pansinusitis but the other received no antibiotic Bacillus subtilis appeared in 4 subjects in the second culturing but in only 1 initially Neisseria catarrhalis disappeared from the 2 persons in whom it was present initially

Bacillus subtilis established itself in the skin of 6 members who did not have an initial culture showing the organism Staphylococcus albus was present in the skin of 7 subjects initially and 4 subsequently (1 member left the party after 5 weeks) Three persons had Staph aureus on the first but not the second determination Two others apparently acquired the organism from the others while with the group Diphtheroids disappeared from 3 and N catarrhalis and Gaffkya tetragena disappeared from 1 each

All but 2 members of the group washed their hands and face almost daily sharing the same wash tin soap and community towel Two members went for 100 days with almost no contact with externally applied soap and water There were no obvious deleterious effects from not washing in the 2 though there were qualitative changes in the population

(4) New England J Med 258 531-533 Mar 13 1958

of skin bacteria Quantitative ob ervations were not made

From 1 subject a skin culture of Staph albu that was not sensitive to penicillin was found but on sub equent culture a penicillin ensitive organism was demonstrated Infectious dise e in the expedition was confined to 2 members One had pansinusiti as well as influenza and the other had a common cold The inu itis (the only infection of probable bacterial origin) occurred in a man who wa hed daily

► [Not a very encouraging report from the viewpoint of manufacturers of toilet soaps? The que tion arises What criteria were u e l to assess the ab ence of obvious deleterious effects—cultural vi ual or olfactory?—E ls]

On the Nature of the Mitsuda and Kveim Reaction R Kooij and Th Gerritsen (Pretoria South Africa) obtained Mitsuda reactions with suspensions of normal liver particles in patients with tuberculoid leprosy These su pensions gave no reactions in patients with lepromatous leprosy The Mitsuda reactions obtained with these preparations of normal tissue containing no leprosy bacilli were similar to those obtained with lepromin containing leprosy bacilli Bacterial filtrates of lepromin and normal ti sue preparations did not evoke Mitsuda reactions in patients with tuberculoid leprosy The authors conclude that the presence of particles is essential for evoking a Mitsuda reaction The *reaction is* apparently a sarcoid (tuberculoid) type of *foreign body* reaction or an isomorphic phenomenon As with *lepromin* preparation of normal tissue can evoke Mitsuda *reactions* in healthy subject The tuberculoid or sarcoid mode of reaction i considered a general predi position of certain per ons The lack of reactivity to lepromin among infants and the gradually developin re pon e among growing children may be a manifestation of a normal maturation cycle Contact with lepro y or tuberculo is i probably unnece sary for development of this reactivity to lepromin

Becau e of the re emblance between lepromin and Kveim antigen everal of the latter were tried on patients with tuberculoid and lepromatou lepro y With Kveim antigen reaction were obtained in patients with tuberculoid leprosy and weak or ab ent reaction in the lepromatous type The Kveim reaction probably differ only quantitatively in healthy per ons and patient with arcoido is leprosy and po sibly ome other disease The Kveim antigen does not appear to contain a specific substance instead the Kveim

(5) D mat log J1 1 J ry 1958

reaction is an expression of a sarcoid mode of reaction in certain persons The authors consider sarcoidosis a syndrome that can be caused by many agents each giving an individual but always sarcoid type of reaction

► [Even the originator of the Kveim reaction do not claim absolute specificity for this test Danbolt (Acta dermat venereol 31 184 1957) for example reported negative reactions only in 46 of 51 nonsarcoid patients and positive reactions only in 41 of 46 proved ca es of sarcoid He also showed that in sarcoid patients reactions were negative with Frei antigen spleen and brain tissue etc Nevertheless it has been claimed by others that positive Kveim reactions could be elicited with entirely non specific material The report by Kooij and Gerritsen claims a similar lack of specificity for the Mitsuda reaction

It seems to us that until really specific test materials free from extraneous substances have been developed the e contradictory results cannot be re solved Whether this will ever be possible for sarcoidosis depends basically on whether sarcoidosis is a disease sui generis or is a reaction form which can be produced by various agents In the meantime it is well to remember that test procedures used every day for other purposes are not 100% specific Despite the fact that the clinician may not know exactly how specific the Mitsuda and Kveim tests are both have proved very helpful The reason for the requirement that large particles be present in the Kveim and Mitsuda skin test materials is not known In serologic test also the size of the antigen particle is important that is why such technics as collodion coating are being used —Ed]

Immunologic Aspect of Sarcoidosis is discussed by Kenneth M Citron[6] (London) Low tuberculin sensitivity i characteristic of sarcoidosis This insensitivity is not an i o lated finding in sarcoidosis but reflects a general deficiency of skin re ctions of the delayed type Poverty of response has been reported to several other antigens which usually elicit a delayed response including trichophytin mumps vi rus and pertussis agglutinogen

In contrast to the poverty of reactions of the delayed type skin reactions of the immediate type or histamine release reactions are normal in sarcoidosis and circulating anti bodies develop normally in response to antigens producing immediate reactions Thus sarcoidosis patients may have ur ticaria angioneurotic edema or allergic asthma

Experiments indicate that failure of the delayed type of immunologic response is due to deficiency of antibody in the skin Diminished production of antibody appear to be the most likely cause of this deficiency in sarcoido is Recent work indicates that there is a relative deficiency rather than complete absence of tuberculin antibody in these patients The use of tuberculin with cortisone and tuberculin in oil

(6) Brit J Derm t 0 48 5 Febr ua y 958

has revealed the pre ence of slight latent tuberculin sensi tivity in many sarcoido is patient

The Kveim test is of great interest in relation to the etiol ogy of sarcoido is The te t material con i ts of a suspen ion of sarcoid ti ue Recently Nethercott and Strawbridge re ported isolation from sarcoid tissue of diaminopiomelic acid and mycolic acid These sub tances are known to occur in mycobacteria but are aid not to occur in normal human ti sue Thi ugge t that the Kveim response might be a tissue reaction to the e bacterial re idue of mycobacteria pre ent in the antigen The suggestion i strengthened by the finding that tubercle bacilli dead or alive B C G or lipo poly accharide of mycobacteria may stimulate arcoid reac tions in sarcoido is

In 49 patients with sarcoido is the proportion with x ray or bacteriologic evidence of previous tuberculous infection was the same in the tuberculin insen itive group as in the group en itive by either the tuberculin test or the more sensitive tuberculin plus cortisone test This is compatible with the view that arcoido is is a manife tation of tubercu lous infection in which depres ed tuberculin sen itivity is a feature of the peculiar ti ue reactivity which determines the development of sarcoido i Thi ob ervation supports a causal relation between tuberculo is and sarcoidosis Why the e patient react to tuberculous infection by this unusual hi tologic and immunologic re ponse instead of by the usual caseating tuberculin po itive reaction remains unsolved

► [The anergy in sarco d i extend to various bacterial and viral aller ge i an l i n t pecific for tubercul n Why *hould the fact that the same* proportion of tuberculin in en itive and tuberculin sensitive sarcoid pa tent have evi lei ce of *previous tuberculou* infect on speak in favor of a co ect o between tube culos and *sarcoido is* The author s findings contrary to h s conclu i n bring no further evidence supporting a rela tionship between these two d eases —F I]

Verrucae Plantares Symptomatology and Epidemiology

Kaj A Ra mussen (*Copenhagen*) tates that within 1 year from October 1951 to September 1952 5,223 new patients with plantar warts were seen at the *Finsen In titute* During the ame period there were 2 284 new patients with extra plantar warts and 4 609 new patients with plantar lesions from pre ure or old patients with recurrences of plantar or extraplantar wart Among the plantar wart patients 44%

(7) A ta d rmat en ol 1 38 pp 39 1958

were preschool children 66 3% were school children and 29 3% were adults Among the patients with extraplantar warts 11 5% were preschool children 42 9% were school children and 45 6% were adults

Among the patients with plantar warts 90 3% had solitary and multiple scattered warts (simple type) 4 7% had mother daughter warts 6 1% grouped warts 2 3% mosaic warts and 0 7% had more than one type Of those with simple warts 57 9% had only 1 wart 19 5% had 2 9 1% had 3 and 13 5% had 4 or more Although in the children both sexes showed equal numbers of plantar warts per patient there were more per patient among adult women than among adult men The forefoot and pulp of the big toe were more often affected in females than in males Tenderness occurred in 76 4% of the patients 17 8% had pain at rest and 19 1% had itching Pain increased with increasing age

The most characteristic diagnostic signs in verruca plantaris were (1) a circumscribing hyperkeratotic ring seen on removal of superficial layers (2) a central bundle of threads running perpendicular to the surface and (3) bleeding on paring the wart down deeply A specially superficial form of plantar wart was seen occasionally in dry plantar skin in which the hyperkeratotic ring was missing Rare cases of keratotic growths were seen in which diagnosis could not be established by clinical examination alone Microscopically some of these proved to be warts others were corns and still others could not be classified The most important lesions to be considered in differential diagnosis of plantar warts are those resulting from pressure (corns calluses and dystrophic pressure lesions) and radiodermatitis

Incidence of plantar warts among patients at the Finsen Institute rose from 33/1 000 in 1925 27 to 425/1 000 in 1948 50 More patients come from the outer districts of Copenhagen than from the inner parts This difference was due to the school children The newer and larger schools are situated in the outer districts and more patients come from large than small schools Patients who did not attend school were evenly distributed throughout the city

Frequency of bathing and of separate washing of feet and the percentage having bath facilities at home were the same for patients with and without plantar warts However fewer plantar wart patients took baths solely at home Among

children who had taken baths at school for less than 1 year there was a relative deficiency of plantar wart patients but among children who had taken baths at school for 1-4 years there was a preponderance of these patients There were more athletes among adult women with warts than with out but among the other groups there was no difference Gymnastics at school were carried out with different kinds of rubber footwear and with bare feet by the same number of persons in the groups with and without verrucae More per sons with plantar warts than without had incurred wounds of their feet within 1 year before attending the clinic Clin ically dermatophyto is of the feet was found in only 1 1% of plantar wart patients In 7 1% of the patients relatives in the home al o had plantar warts

Ra mussen concludes that communal baths at school are the chief source of plantar wart virus infection and are re sponsible for the marked increase in incidence Wearing of rubber footwear and traumatization of the feet by doing gymnastics barefoot do not appear to lower resistance to the plantar wart virus The increased incidence of plantar warts on the forefoot in women may be due to the increased pres sure on this part of the foot resulting from wearing higher heel This is the only auxiliary cause for the appearance of plantar warts uncovered by thi study

The most import int prophylactic measure in the control of plantar warts eems to be exclusion of patients with these le ion from communal baths

► [This 146 page monograph on plantar warts describes in detail the or gani ation of the project and the method of collecting data. In addition there a e comprehensive chapters on symptomatology and epidemiology as well as a final chapter devoted to discussion Suggestions as to prophy laxis are presented but therapy is not discussed. This is indeed a very comprehensive stu ly based on many years of work and a review of con siderable material Rasmu sen s conclusion that exposure to common baths at chool s a major source for infection with plantar wart virus is in keep ng w th opinions of other All tho e interested in this problem should efer to the original treatise —Ed]

Incidence of Verruca Plantaris (Plantar Warts) in School Population In a survey of 2 742 intermediate and high school students in 4 chool J J Gasse and R I Miller[8] (Jack on Mich) found plantar warts in 105 (3 8%) There was no dif ference in the attack rate between boys and girls but the in cidence of plantar warts in one school was significantly higher than in the other 3 studied

(8) A h Ped t 75 79 84 J ly 1958

A careful survey of the physical plant and athletic programs at all 4 schools revealed several factors which might help to explain the higher incidence of plantar warts at one school (School A) At this school there was emphasis on an outdoor type sports program The program was largely conducted on a blacktopped playground and many of the students wore thin soled footgear while engaged in activities on the hard surfaced play area There was less emphasis on swimming activities at School A The students however used hopelessly crowded shower and locker room the floors of which were constantly wet It was almost impossible for them to dry their feet thoroughly after showering From the locker room to the showers the students traversed barefooted an area used by other classes on their way to and from the playground This area became wet and muddy and could not be kept clean

In School B and School D showering and dressing facilities were also crowded but floor drainage was much better The emphasis at these schools was on pool activities rather than play on hard surfaced playgrounds At School C there was a modern pool tile floors were well ventilated and outdoor activities were conducted on sodded play area

► [Obviously opportunity for exposure to wart virus is one of three important factors which determine the incidence of verruca plantaris The second factor is individual susceptibility to infection with the virus clinical experience shows clearly that some persons have a much greater susceptibility than others We also have had the impression that susceptibility to wart virus infection is greater in some families than in others Familial susceptibility is difficult to assess however since there is always associated the increased opportunity for exposure among members of the family The third important factor is trauma and pressure which probably are among the decisive factors in determining the localization of wart —Eds]

ECHO 9 Virus Exanthema James T Prince Joseph W St Geme Jr and William F Scherer[9] (Univ of Minnesota) report that a generalized morbilliform rash lasting 1 3 days became epidemic in Minnesota in 1957 Some patients had fever Commonly infection spread within families and within neighborhoods Though rash alone was frequent symptoms ranged from inapparent infection through skin rash with little disability skin rash and fever skin rash and aseptic meningitis and finally to aseptic meningitis without rash

Each strain of virus isolated from patients was identified by appropriate neutralization tests and acute and convalescent phase human serums were assayed for neutralizing an

(9) J A M A 16 691 696 June 7 1958

tibodies The pathogen was thu found to be a strain of the enteric cytopathogenic human orphan viru ECHO 9 It resembled the prototype ECHO 9 in its behavior in cultures of cells from monkey kidney human amnion and the HeLa strain of human carcinoma but it was al o pathogenic for newborn mice and for tissue cultures of human fore kin cell In its pathogenicity for newborn mice it resembled certain European English and Canadian strains of ECHO 9

The striking change in capacity of Minne ota ECHO 9 to produce di ea e in mice or de troy foreskin fibroblasts in culture apparently was conditioned by passage of the viru e in primary monkey kidney cultures A single passage in monkey kidney cell cultures could have produced such change by increasing the concentration of virus and/or inducing or permitting a qualitative change in virus properties

The incidence of di ease from ECHO 9 virus in Minne ota was estimated by the Minnesota Department of Health Instances of aseptic meningitis with or without exanthema were determined by canvass of 400 hou eholds randomly selected Projection from survey findings suggested that over 200 000 case of ECHO 9 virus infection occurred during the summer of 1957 in the Minneapolis St Paul area and that a many a 400 000 cases occurred in the whole state

The e tabli hment of an etiologic relation between ECHO 9 viru and exanthema should not lead clinicians to the general conclu ion that all summer rashes are caused by this virus Such a conclusion would not be valid even were an epidemic of ECHO 9 virus induced di ea e existent in a community Evidence against such a conclusion is pre ented by finding in 4 patients who had a skin rash indi tinguishable from that cau ed by ECHO 9 virus but who failed to yield laboratory evidence of ECHO 9 virus infection

► [Most phy sician u loubtedly ou1d have difficulties differentiating this di ea e from others with a morbilliform rash unless hey were in a region in which ECHO 9 irus was known to be e demic or epidemic or unless the erupti n were associated w th men ngit s —Eds]

Erythema Infectiosum Report of Outbreak in Marshfield Wisconsin i pre ented by Kenneth K Wilcox (Wisconsin State Board of Health) and Alfred S Evans[1] (Univ of Wi consin) During 13 weeks 62 cases were found in which a rash occurred imilar to that seen in erythema infectiosum Patients were aged 2 16 and 75% were girl The cutaneous

(1) Wiscon M J 5 10 114 M h 19 8

eruption had two distinct patterns Some children showed a diffuse erythema of the cheeks with a suggestion of perioral pallor All had an erythematous maculopapular rash primarily on the extremities but to some extent on the upper chest and back The striking and highly characteristic feature was a reticular lacelike or geographic appearance This rash was transient becoming more marked it covered by a warm hand or if the patient perspired There was questionable redness of the throat in a few patients No conjunctivitis Koplik s spots pharyngeal exudate posterior occipital adenopathy or bronchitis was noted

The rash lasted 1 14 days The mean and mode both fell between 3 and 4 days The rash tended to disappear and reappear during the course of the disease Mild itching was noted in 13 cases Few patients had symptoms associated with the cutaneous eruption Two recurrences were noted but observation was not long enough to include late recurrences Multiple cases in a family were frequent

A cytopathogenic agent was obtained in human fibroblast cultures inoculated with fresh unfrozen throat washings and stool suspensions Since more fibroblasts were not immediately available it was necessary to freeze the first passage at —20 C for over 3 weeks before a second passage could be made No cytopathogenic agent was then recovered in the second passage The cytopathogenic agent was probably labile and lost by freezing and storage

► [Erythema infectiosum apparently is not generally recognized as such by physicians when they see isolated cases This supposition is supported by the fact that persons older than 16 manifest relative immunity probably as the result of having had an undiscovered infection with erythema infectiosum during childhood or adolescence and having become immune at that time —Eds]

Eruptive Dermatosis of Extremities Probably of Viral Origin was observed sporadically during the past few year in 11 children aged 9 months to 9 years by A Crosti and F Gianotti[7] (Univ of Milan) The clinical history in these patients included rhinopharyngitis or mild bronchitis not directly related to the cutaneous eruption weakness digestive disturbance and slight fever thick eruption of lentil sized erythematous papuloid lesion copper to wine red with some purpuric suffusions especially on the legs typical distribution over exposed portions involving only arm

(7) Dermatologica 115 671 67, November 1957

and legs neck and face (Fig 52) In the lower extremities the eruption involved the superior iliac border of the buttocks posteriorly and the inguinal groove anteriorly it reached the humeral girdle in the upper extremities and the jugular border in the neck It showed ascending progression beginning in the legs The face was the part least involved In some cases the lesions were confluent on the knees and elbows or in previously traumatized areas Skin folds were



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the lea t affected Mucosas were spared except in a ca e in which there wa an erythematous macular appearance in the buccal muc sa The eruption progressed to completion in a few day and did not increase but persisted 30-70 days Resolution wa accompanied by moderate lamellar desquamation and there were no recurrences

The cutaneou syndrome wa accompanied by superficial polyadenopathy with hard freely movable and nonpainful lymph node There was no splenomegaly the liver projected beyond the co tal arch During the course of the disea e follicular or herpetic angina or episodes of diarrhea were ob erved Hi tologically there were slight hyperkerato si and parakerato is and diffu e monohistiocytic infiltration of dermal capillaries and at the dermoepidermal border

Clinical and laboratory findings were frequent vascular fragility with petechial eruption negative skin reactions to

tuberculin streptococcus and staphylococcus moderate hypochromic anemia slight leukocytosis or leukopenia with monocytoid histiocytic elements (2 15%) Turk cells and plasma cells Myelograms (6 cases) showed definite increase of histiocytes analogous to those in the peripheral blood Erythrocyte sedimentation rate antistreptolysin titer and Paul Bunnel Davidsohn reaction were normal Cold agglutinins were absent in the serum Electrophoretic analysis showed increase in alpha and beta globulins and sometimes of gamma globulins

This exanthema is definitely different in duration type and location from ordinary infantile exanthemas and in absence of lymphocytosis and splenomegaly from infectious lymphocytosis It resembles more infectious mononucleosis which however shows more varied mobile and transient lesion less characteristically localized as well as splenomegaly and a positive Paul Bunnel Davidsohn reaction

► [Dermatoses in children which have failed to conform to the typical pictures of commonly known exanthems have been noted in this country Where drug etiology and so called toxic causes have been ruled out pediatricians also have tended to attribute these eruptions to a viral origin —Eds]

Larva Currens Distinctive Variant of Cutaneous Larva Migrans Due to Strongyloides Stercoralis Robert P Arthur and Walter B Shelley[3] (Univ of Pennsylvania) report a case

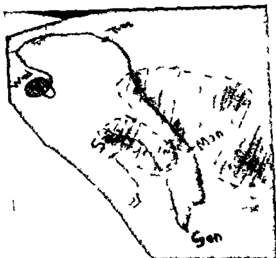
Woman 46 had had a pruritic erythematous urticarial lesion on the medial aspect of the left midthigh for 2 weeks The eruption progressed from time to time in an irregular serpiginous linear fashion Treatment with systemic streptomycin chloramphenicol erythromycin and penicillin was without effect First examination showed a raised urticarial band surrounding a fine distinct erythematous central linear lesion The central line extended a short distance ahead of the developing urticaria It was possible to see the lesion advance after a period as short as 10 minutes After several hours the lesion ceased moving only to resume movement the next day Within a 5 day observation period the active end of the lesion advanced 7 11 cm daily during a few hours out of each 24 (Fig 53) The urticaria subsided slowly leaving a distinct brownish track

The patient denied any travel animal contact or previous helminthic disease She recalled having cleaned unwashed and contaminated celery a short time before onset of the eruption A diagnosis of larva migrans was made and the advancing end of the lesion was sprayed with ethyl chloride to the point of blister formation This treatment on two occasions did not stop the progress of the larva However a single intradermal injection of crystalline lyophilized

(3) A M A Arch Dermat 8 187 190 August 1959

tryp in (1 ml of a concentration of 10^3 in isotonic saline) at the mo t advanced point of the lesion proved curative

Larva migrans due to intracutaneous S stercoralis larvae i known to the parasitologist and tropical phy ician but ap parently i unknown to the dermatologist All reported ca e have shown perianal topography unusual urticarial re pon e and extremely rapid advancement of the burrow



F g 53 —Rout f la m pped on l f med l th gh Not p d p g f le m y g f om 11 m i w hou ly p rt da H t h d f ffect b l ble (h h l ei l t t wh h la w t pped b jec m f t st t d rm lly Th g ph w t k (rt h l l d d) ep en t m f l m (Court y f Arthu R P d Sh l W B A M A A h D m t 8 1 6 190 A g t 1958)

Proved ca e have invariably pre ented evidence of chronic inte tinal trongyloidiasis

Strongyloide tercoralis i one of the true un egmented *roundworm* It parasitizes the inte tinal tract a an adult fe male worm mea uring about 2 mm long and only 50 µ wide The ova may hatch within the muco a of the mall bowel into a noninfective larval stage Later tiny filariform larvae may develop in the intestine or on fecally contaminated skin The e la vae ecrete proteinase collagena e and other en zymes which permit penetration of the normal intact epi dermis and corium They then go into the circulation and via the lung back into the inte tinal tract The reinfection accounts for a unique feature of larva migrans due to this

organism i e, its localization and recurrence Strongyloidiasis is endemic in warm climates and occurs in man but is rarely found in dogs and cats Relatively asymptomatic chronic infections occur with eosinophilia as the solitary clinical feature The new anthelmintic dithiazanine is effective against strongyloidiasis

The name larva currens is proposed to point up the distinctiveness of the dermatologic patterning of cutaneous strongyloidiasis Trypsin was used in treating the present infection because of the known lethal effects of all proteolytic enzymes on many nematode infections of the intestine

► [The authors propose the Latin term larva currens which means racing larva to point out that this form of larva migrans is unique in its rapidity of movement as contrasted to others In this case the diagnosis was established on the basis of clinical appearance and course of the disease It would have been interesting to see the results of stool examinations which presumably would have led to demonstration of the larvae —Eds]

Endemic Cutaneous Leishmaniasis in France appear to be limited to the Mediterranean coast with an endemic area in Languedoc and Roussillon Since 1951 P Kimbaud J A Rioux and F Duntze[4] (Montpellier) studied 8 cases in which the diagnosis was confirmed and 2 others seen after a therapeutic test The actual number of cases is probably greater than reported since some lesions seen by general practitioners probably escape detection The oriental sore in this region is atypical it develops slowly without subjective signs and displays a tendency to spontaneous cure after many months Even when the diagnosis is suspected search for the parasite is sometimes negative in old lesions

Oriental sore is caused by a protozoa of herpetomonas type the Leishmania tropica related to but different from L donovani which is responsible for kala azar Epidemiologically it is assumed that the disease affects animals primarily but produces an occasional isolated case in humans Wild fowl and dogs are suspected Localization of lesions on exposed parts indicates inoculation by a stinging insect Phlebotomus papatasii a Mediterranean species is the principal vector

The lesions are situated exclusively on the face particularly on the protruding portion of the cheek They may be observed at any age (2 80 years in this series) The incubation period is difficult to estimate since usually the time of the in

(4) Presse m d 66 89/ 898 May 1 1958

fecting sting is unknown In 1 case affecting the lower lid it was known to be 15 days The lesions are always solitary not painful nonsuppurative and develop slowly Morphologically they are of four types lupoid furunculoid infiltrating or ocular After 1 1½ months progressive growth the lesion becomes stabilized and remains resistant to all nonspecific therapy recurring in situ even after radiotherapy or electrocoagulation This fixed nature of the lesion without any tendency toward extension is of prime importance in diagno i In some patients the lesion had been present 9 months to 3 years before it was correctly identified

In fresh lesions a stained smear or histologic section reveal an abundance of L tropica but in old lesions the parasites are often difficult or impossible to find The histologic structure is that of an inflammatory granuloma in the epidermi there are papillomatosis and marked acanthosis especially at the edge of the ulcer Infiltration of the dermis is inten e with polynuclear neutrophils and eosinophils and histiocytes Organisms are found within the histiocytes and also free in the dermis

Antimony treatment is rapidly effective if the lesion is recent The authors generally used 2166 RP (glucantime) in an average do e of 0 1 cg /kg in a course of 12 intramuscular injections given daily or 3 times weekly If cure is not complete a econd course can be given after a few weeks No seriou side effect have been observed In 1 patient local injection of emetine cured the lesion in 1 month

Cutaneous Amebiasis Clinical and Anatomicopathologic Study Skin conditions caused by Endamoeba histolytica may be cla sified into true cutaneous amebiasis in which the protozoon i present and dermatoses (amebides) in which the protozoon is never found in the skin lesions True cutaneous amebiasi i rare G Pozzo and R Rabotti (Univ of Milan) describe the first case reported o far in Italy

Man 38 had a history of exudative pleurisy and untreated dysentery diarrhea At ag 22 le ions of a papillomatou type in the anal and perianal region were treated surgically without much success At 28 lesions of the same type appeared on the prepuce and at 30 besides a recurrence of the same le ions in the anu perianal area and prepuce the fir t le ion of papillomatous granulomatous type appeared on the anteri r portion of the hard palate On examination vegetative and granulomatous lesions were found on the face 5th toe anal and perianal regions and prepuce (Fig 54) With irradiation and an

(5) Chir [illegible] d rmat f 99 40 74 31 Ap 19 8

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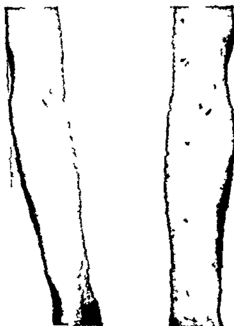
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(4) Presse méd 66 897 898 May 21 1958

Man 35 had had a highly pruritic papular dermatitis for 2 months The eruption consisted of groups of papules and vesicopapules 1-5 mm in diameter occurring mostly on the left arm and forearm (Fig 55) left thigh and leg and left side of the trunk The lesions resembled insect bites The patient had a cat which had started to scratch itself and began to lose hair about 2 months previously He also noted that papules appeared on his skin soon after contact with the cat

Examination of the cat revealed the presence of a mite which was identified as *Cheyletiella parasitivorax* An itching papule appeared on the patient's skin about ½ hour after a mite was placed on his fore-



[illegible] (Courtesy of [illegible]) 1957 [illegible]

arm Even after prolonged contact with the cat the patient's wife showed no mite bites After treatment with DDT powder the cat stopped scratching and the patient's dermatitis cleared

Cheyletiella parasitivorax has been found chiefly in the fur of rabbits and hares but occasionally also on cats and dogs In some instances the mite causes no irritation of the skin of the host in others itching occurs as in this case

* [The failure of some persons including the patient's wife to react to the mite is noteworthy Probably those who react have undergone allergic sensitization to the mite or its products — Eds]

tibiotic and hormonal treatment the lesions of the face regressed slightly Later they progressively extended to the central regions of the face The dermatosis then became infiltrative destructive and phagedenic and resulted in massive cutaneous muscular and bony destruction The patient general condition deteriorated and a severe anergy was thought to be responsible for the spreading of the condition and its destructive phagedenic aspects

Reactions to tests for syphilis negative until the patient was 30 became suddenly strongly positive with all antigens and at first were not modified by intensive therapy Sedimentation rate was high Biologic tests on various animals cutaneous and intradermal injection with numerous antigen and cultures on various mediums always gave negative results In the terminal stage E histolytica was found microscopically in biopsy specimens from the ulcerations Histo



Fig 54 —Localization of vegetative and granulomatous lesions ... objective findings on admission to clinic (Courtesy of ... and Rabett R Gior ital dermat ... 99 40 4 Mar Apr 1958)

logic study of biopsy specimen of granulomatous tissue from various areas always showed massive epithelial ulcerations small ulceration and marked inflammation In the fibrinous necrotic matter of the ulcerations were epithelial fragment infiltrate mainly leukocytes and inflammatory element On emetine treatment the skin lesions improved but the general condition was extremely poor and the patient died

It is suggested that the massive symmetrical destruction of facial skin muscle and bone was due not only to the lytic action of E histolytica but also to a trophic disturbance very likely of nerve origin

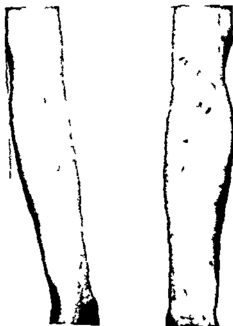
► [Patients complaining of or giving a history of dysentery who present anal or perianal ulceration or papillomatous or granulomatous lesions should be investigated for amebiasis —Ed]

Dermatitis Caused by Mites (*Cheyletiella Parasitivorax*) Living on Cats Veikko Pirila and Ali Marjoma[8] (Univ of Helsinki) report a case

8 ... 351 19

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F g E pt n on l f f m (C rtes f P l V d M m A Arta de t col 3 3 6 38) 1937

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Pigeons Acting as Vector in Acariasis Caused by Dermanyssus Gallinae (DeGeer, 1778) Gerard A. DeOreo[7] (Cleveland) reports 14 cases of acariasis due to D. gallinae (the chicken mite) with the pigeon acting as the source of the mites. *In 7 patients the offending mites were found and identified as D. gallinae. In the other 7, pigeons were found in each instance nesting on or within a few feet of their homes; however mites were not available for identification.* The mites hide during the day and feed at night.

The commonest lesion seen in these patients was an erythematous papule, usually about 1 cm. in diameter and resembling a mosquito bite. A tiny hemorrhagic punctum could be detected in the center of the lesion. The dermatitis was characterized by clustering of 3-6 single papules. Occasionally vesicles were observed; less often large urticarial plaques. *Papular urticaria was seen in 2 children. Secondary pyoderma occurred in 2 patients. Chronic irritation produced localized neurodermatitis in 2 others. An infant had a generalized toxicoderma associated with mild constitutional reactions.*

Successful treatment depends on recognition that the common pigeon may be the source of avian mites in patients with bites resulting from arthropods. Increased interest in mites as vectors of disease in man and domesticated animals has led to the development of many potent acaricides including chlorophenothane (DDT), chlordane and lindane. An emulsion containing benzoate, benzocaine and DDT is a useful repellent when applied to the skin.

► [A probably much overlooked dermatitis. Pigeons on roofs and window ledges are indeed common in New York. The modern air conditioner which extends outward from the window frequently may well provide space between it and the window ledge for nesting pigeons. Dermanyssus gallinae might invade the air conditioner and literally be blown into the room together with the fresh air.—Ed.]

Pyoderma Gangrenosum Associated with Hypogammaglobulinemia. Report of Two Cases is presented by David Bloom, Dorothy Fisher and Marvin Dannenberg[8] (New York Univ. Post Grad. Med. School and Bellevue Hosp.).

CASE 1.—Woman, 50, had had an eruption for 2 years. Exacerbations occurred from time to time during the next 2 years despite antibiotics given orally, injections of Staphylococcus aureus vaccine and local treatment with streptokinase-streptodornase, zinc peroxide and electrode iccation. Recurrences of pyoderma vegetans ceased en

(7) A.M.A. Arch. Dermat. 77: 427-429, April 1958.
(8) Ibid., pp. 412-421.

tirely after injections of gamma globulin Three series of 4 injection each given every other day with each series totaling 40 cc. were given within a month One month later 8 weekly injections totaling 40 cc were given

CASE 2—Man 55 had been observed for several years and had responded temporarily on several occasions to antibiotic and general supportive therapy After large dose of gamma globulin blood transfusions and supportive and steroid therapy the progressive and extensive ulcerations epithelized and there was almost complete cessation of recurrence of the eruption Initially gamma globulin was used in doses of 5 cc twice a week but when the dose was finally increased to 20 cc twice a week improvement was more rapid

In contrast to agammaglobulinemia which is frequently associated with absence of circulating antibodies and with a low titer or complete absence of isohemagglutinins in hypogammaglobulinemia the immunologic mechanism are not completely paralyzed though there may be a reduction of antibodies and a low titer of isohemagglutinins Thus the second patient reacted to tuberculin and smallpox vaccine and the isohemagglutinins were within normal limits though of low titer The bone marrow which in agammaglobulinemia shows absence of plasma cells was normal

Ulcerative colitis or any other visceral disturbance if present is not always the cause of pyoderma gangrenosum It is assumed that both the visceral and cutaneous involvement are due to weakened immunologic resistance of the host The finding of hypogammaglobulinemia associated with pyoderma gangrenosum may be a forward step toward elucidation of the low resistance of the host in pyoderma gangrenosum Future investigation will possibly lead to discovery of other immune mechanisms and their defects in this disease thus explaining more fully the state of weakened resistance of the host since hypogammaglobulinemia appears to be only one of many factors which determine the low resistance

Steroids may be of value in controlling ulceration in pyoderma gangrenosum Therefore their administration should be tried in connection with other supportive therapy and antibiotics The explanation given by Wright and Greco for the beneficial effect of steroid in some cases of pyoderma gangrenosum viz that some harmful violent antibody reaction may be suppressed by the hormone seems logical

► [We had the opportunity to observe the astonishing improvement and healing of the deep ulcerations in the author Case 2 The optimal treatment for cases of pyoderma gangrenosum at present apparently is combined corticosteroids and gamma globulin—Eds]

Pyoderma Gangrenosum with Unusual Syndrome of Ulcers Vesicles and Arthritis Samuel Ayres Jr and Samuel Ayres III[9] (Los Angeles) report 4 cases Each patient had typical chronic *recurrent spreading ulcers with raised purplish borders* and erythematous halos All had fairly severe chronic arthritis and in 3 it was of the rheumatoid type No patient had evidence of ulcerative colitis or other debilitating disease Two patients had a superficial cutaneous eruption resembling dermatitis herpetiformis The eruption was symmetrical pruritic and consisted of crops of vesicles



Fig 56—Vesicular lesions and scars on left knee and thigh (Courtesy of Ayres S Jr and Ayres S III A M A Arch Dermat 69 80 March 1954)

(Fig 56) vesicopustules papules and crusts A third patient had had crops of blood blisters All patients were benefited but not cured by sulfapyridine or salicylazosulfapyridine Benefit included response of vesicular lesions as well as ulcers and in 1 case there was also improvement in the arthritis

Vesicular eruptions resembling dermatitis herpetiformis in association with pyoderma gangrenosum have been previously reported *with control* of both the ulcerative and vesicular lesions with sulfapyridine Arthritis associated with ulcers has been mentioned by a number of authors but has never been emphasized except *in a report by Perry and* Brunsting in which arthritis occurred in slightly more than half of 19 cases

(9) A M A Arch Dermat 77 69 80 March 1958

It is curious that an eruption which looks so much like dermatitis herpetiformis should also respond to the one drug which uniquely benefits that disease at the same time sharing the benefit with the ulcerative lesions This has caused the authors to wonder whether the ulcerative lesions might represent an aberrant form of dermatitis herpetiformis

The concept of pyoderma gangrenosum has been broadened to include symptomatology and therapeutic responses not originally contemplated in earlier reports The essential cause or causes remain unknown The authors agree that the disease is not primarily a local infection and does not necessarily depend on an underlying debilitating condition such as ulcerative colitis or other infection

► [Lupus erythematosus dermatomyositis psoriasis Reiter s disease allergic purpura and serum sickness type urticaria are among the dermatoses in which joint involvement may characteristically occur

Of particular interest in these cases is the development of an eruption closely resembling dermatitis herpetiformis Similar eruptions have been seen in encephalitis (personal communication from Dr H Brodhagen) and also in Hodgkin s disease after x radiation The question arises whether the mechanism producing dermatitis herpetiformis sui generis and the dermatitis herpetiformis like eruptions accompanying other diseases is the same The fact that both syndromes respond to sulfapyridine therapy suggests that this may be so at least in some instances

How does sulfapyridine exert its favorable therapeutic effects in dermatitis herpetiformis Is it an antibacterial antiviral or other antimicrobial effect The fact that the eruption can be controlled in some patients for many years on such small doses as 0 5 Gm sulfapyridine daily (see Cooper M U S Armed Forces M J 9 910 1958) might be considered to speak against this possibility The mode of action of the sulfonamides is made even more puzzling since certain other apparently nonantimicrobial compounds which have a pyridine ring but which are not sulfonamides (e g nicotinic acid) are effective in some cases of the disease as are some sulfonamides and sulfones which do not contain the pyridine ring

Stoughton has shown that an enzyme present in the intestinal wall of patients with ulcerative colitis is capable of producing acantholysis type vesiculation in the skin of man Perhaps the efficacy of sulfapyridine in ulcerative colitis and in the dermatitis herpetiformis like eruptions associated with it is based on some interference caused by the sulfonamide with the activity of this enzyme —Eds]

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13 VENEREAL DISEASES OTHER THAN GONORRHEA

Should Premarital Blood Test Be Compulsory? Using syphilis morbidity in the infectious stage and syphilis mortality in infancy as two measures of the decline of syphilis during the past 2 decades A W Hedrich and Charlotte Sil

verman[1] (Maryland State Dept of Health) point out that there has been a tremendous decrease in recently acquired syphilis in *the country as a whole The percentage decline* has occurred equally in states with and without a compulsory premarital blood test law This suggests that the compulsory premarital blood test laws exert little influence on *syphilis mortality and morbidity* Other factors such as prenatal blood testing improved case finding and particularly penicillin treatment have more likely been responsible for the rapid decline in syphilis Premarital blood testing reveals so few infectious cases of syphilis as to make it an unproductive as well as an enormously expensive method of case finding Added to these deficiencies is the increasing problem of false positive reactions in blood tests which will become even more serious as syphilis declines further Compulsory premarital blood test laws may create more penalties than benefits for the population and can no longer be justified

► [We share the opinion of Hedrich and Silverman and others that com*pulsory premarital blood testing should be abandoned The article points* out that the cost of finding 1 infectious case of syphilis by this method now probably exceeds $25 000!—Eds]

Epidemiology of Syphilis Causal Factors in Present Tendency Toward Its Recrudescence evident since 1955 are discussed by A Touraine[2] (Paris) Although until *1954* there was a considerable decrease in the incidence of syphilis this was not so great as indicated by the statistics usually cited which give reductions of *66 92%* depending on the country These figures compare the period of *1943-47* with that of *1952 55* *i e* the base used was a period of increased incidence owing to World War II To be more exact comparison should be made with the period of 1930 39 during which syphilis was considerably more stable and exposed to normal social conditions When this period is used as a base for comparison, the decrease in syphilis is not over *26 80%* The recent decrease in incidence of syphilis may be no more than one of the many *fluctuations* exhibited by this pandemic every 8 15 years Serologic investigations show that acquired latent and congenital syphilis have decreased less than clinical reports would indicate Syphilis appears definitely to be increasing since 1955 to judge by the growing number of primary and secondary cases registered by sev

(1) Am J Pub Health 48 1 5 13 February 1958
(2) *Presse med* 65 1851 1854 Nov 16 195

eral countries despite their vigorous antivenereal disease programs

Factors capable of causing a recrudescence of syphilis are always present Some are inherent in the population of a given country Of these some causal factors are individual and relatively less important such as negligence in hygiene and physicians who fail to recognize syphilis or fail to participate in the campaign against venereal disease General factors are more important Some of these are tied up with economic conditions In periods of prosperity prostitution and venereal disease flourish in periods of depression prostitution and syphilis decrease Great movements of population always favor outbreaks of syphilis as illustrated by wars universal expositions etc

Certain social classes are more affected than others and for this reason more dangerous for the whole population e g prisoners foreign travelers and clandestine prostitutes General welfare demands an attempt to reduce these factors of pollution and most so called civilized countries have developed antivenereal disease campaigns which should be maintained and strengthened

Important endemic areas of syphilis persist in various parts of the world and affect a fourth to over half of certain groups These areas have been studied and mapped and collective measures have been instituted These studies have shown that Bosnia Madras South Africa and Tahiti are among the regions where syphilis has not decreased Each country should protect its frontiers by rigid control of immigration from these dangerous endemic areas

Prevalence of Venereal Disease in Prostitutes Results of examination of women arrested on charges of prostitution in New York City during 1950 56 were analyzed by Theodore Rosenthal and Jules Vandow[3] (New York City Dept of Health) and compared with similar data obtained during 1936-46 The number of prostitutes arrested annually decreased 49% from 1940 to 1952 but increased 26% from 1952 *to 1956* During the past 10 years the number of white women arrested declined *73 2%* but the number of nonwhite women declined *only 24 6%* *Of the* white women arrested one fifth were aged 20-25 and another one fifth 25 30 Of the nonwhite

(3) Brit J Ven. Dis. 34 94 99 J 1958

women arrested, one third were aged 20 25 and one third 25 30

There was a marked decrease in the number of women found to be infected with gonorrhea only 5 2% in 1956 compared with 23 6% in 1946 In 1956 35 7% were infected with syphilis in 1946 21 3% were infected and in 1956 only 8 5% During 1942-46 186 cases of infectious syphilis were found (0 8% of the women examined) whereas during 1952 56 only 5 women had infectious lesions (0 04% of the women examined) The proportion of patients with latent syphilis fell from 22 7% in 1946 to 4% in 1954 However in 1955 the proportion had risen to 7 9% and in 1956 to 10 5% These increases have coincided with an increase in the number of women brought to court in the past 2 years

In New York City the prostitute plays a lesser role at present in the spread of venereal disease than the promiscuous amateur In 1943 and 1944 3 625 contacts classified as friends were examined and 54% were infected with venereal disease Of 474 contacts classified as pick ups 52% were infected as were 55% of 58 contacts described as prostitutes but not arrested In the first 4 months of 1957 60 9% of 2 213 contacts classified as friends 44 7% of 441 contact classified as pick ups and 51 5% of 33 contact classified as prostitutes but not arrested were found to have venereal disease

► [The fact that prostitutes in New York City nowadays are less of a venereal disease threat than amateurs represents a striking sociologic development —Eds]

House to House Serologic Survey with Multiphasic Screening was conducted by the New York City Health Department in the Harlem section of Manhattan over a 10 week period in 1955 According to Theodore Rosenthal and Jules E Vandow [4] 23 675 persons were tested for syphilis Of 3 406 persons with positive or doubtful blood tests 2 116 reported to the health department clinic and underwent a multiphasic screening procedure This included a complete physical examination repetition of the blood test genital smears for gonorrhea urine examination for sugar chest x ray and Papanicolaou smears of the cervical secretion (in women over 21)

Of the 23 675 persons tested 14 872 were nonwhite 6 701 whites and 2 102 (mostly Puerto Rican) could not readily be

(4) Pub Health Rep 7 969 975 November 195

classified racially The reactivity rate to the serologic test for syphilis for the entire group was 14 4% Syphilis was found in 1 918 per ons or 8 1% of those tested 406 were new cases 911 were patients requiring further treatment and 601 had been adequately treated Syphilis was twice as preva lent in nonwhites as in Puerto Ricans Reactions considered a fal e positive apparently occurred in 31 7% of the Puerto Rican reactors—3 times the percentage found in nonwhites

It is estimated that 14 771 nonwhite in the Central Harlem District are in need of antisyphilitic treatment In the two areas of East Harlem te ted 1 235 Puerto Ricans are in need of this treatment

Multiphasic screening of the reactors resulted in finding 18 per ons with gonorrhea 23 with previously unknown di abetes 13 women with squamous cell carcinoma of the cervix 5 with active pulmonary tuberculosis and 20 with heart or lung conditions These results confirm the value of multi phasic screening procedures in su pect neighborhoods

► [The h gh incide ce of syphilis did not come as a surpri e since the particular health d strict canvassed was known to have a particularly high syphilis ate It would be interesting to know the total co t of such a stu ly n ver 23 000 unselected subjects —Ed]

Results of Therapy of Latent and Asymptomatic Syphilis in Prison Population II Seroreversal Following Definitive Treatment as Shown by New York State Complement Fixation Test was studied by Bernard I Kaplan James Ryan Evan Thomas John C Cutler and Oscar Jones in 2 820 patient The rate of seroreversal as measured by th single procedure was slow reaching 25% after 5 years and 50% after 11 years observation One year after the first complete evalu ation tests of only 1% of patients with syphilis of 4 or more year duration had become negative as compared with those of 14 of patients with syphilis of less than 4 years duration At 2 years observation the rates were 5 9 and 23 7% re pectively

The long duration of po itive tests in patients adequately treated for latent syphilis shows the futility of repeated cour es of therapy given in hopes of achieving a further precipitous fall in the serologic test for syphilis (STS) or of accelerating the achievement of seronegativity in persons with persistent eropositive findings after an initial ade quate schedule of penicillin or chemotherapy 1 or untreated

(3) J Chronic D 7 312 3 0 April 19 8

patients who have achieved and maintained the status of latency for a period of years, therapy should be given expressly to prevent late manifestations in those who have not undergone spontaneous cure but whose status with respect to Treponema pallidum cannot be determined by any antemortem method now known Such therapy should be understood to have little or no effect on the achievement of seronegativity

In latent as in early syphilis the curve of the serologic fall of the given patient is often not smooth The fluctuating nature of the STS depends on many factors in the patient and in the laboratory This must be recognized for what it is and a single increase in titer should not be interpreted as an indication for further treatment on the assumption that a serologic relapse is occurring

Diagnostic Significance of Herxheimer's Reaction in Primary Preserologic Syphilis was studied by Frances Albertazzi[6] *(Univ of Turin)* *Sodium penicillin 100 000 units was given intramuscularly to 17 hospitalized patients with untreated primary syphilis in the preserologic stage after which the temperature curve was studied* The antibiotic caused intense general reactions (headache myalgia malaise) in all patients after 4 5 hours and the temperature rose to 100 4 102 2 F in 9 patients and to about 104 F in the others after 7 8 hours All symptoms subsided within 12 14 hours Although the serologic tests remained negative while the temperature was high they because positive after varying intervals of time (in 6 patients 48 hours after injection)

Appearance of the positive reaction is ascribed to the powerful antispirochetal action of penicillin which on liberating massive doses of antigen stimulates the production of reagins capable of conditioning a positive serologic reaction

Because relatively small doses of penicillin caused a marked febrile reaction in all these patients it is concluded that when for various reasons a *clinical diagnosis of primary syphilis in the preserologic stage cannot be established bacteriologically, Herxheimer s reaction caused by injection of a small dose of penicillin can be a valuable diagnostic tool* The definitive diagnosis can be confirmed as the clinical and serologic findings become evident

(6) Minerva dermat 33 265-267 July 1958

Effective Simplified Serologic Test for Syphilis Employing Reiter Protein George H Kostant and Louise C Kelcec[7] (New York Univ Post Grad Med School and Skin and Cancer Unit) evaluated the Reiter protein complement fixation test (RPCF) using the soluble thermolabile protein fraction of cultured Reiter treponemes as antigen in 61 patients with treated and untreated early syphilis 95 with late and late latent syphilis 21 with central nervous system syphilis and 17 with congenital syphilis The specificity of the procedure was also evaluated in 41 normal seronegative patients and 167 nonsyphilitic biologic false positive reactors Comparison of the sensitivity and specificity of the RPCF with the Treponema pallidum complement fixation test (TPCF) was the prime objective of the evaluation since the technics of the two procedures are identical in that the one fifth volume Kolmer Wassermann technic is used in each

Results of the study indicate that the RPCF compares favorably in sensitivity with the TPCF using a desoxycholate aqueous extract of the virulent Nichols strain treponeme as antigen The specificity of the RPCF in this study was 100% as there was no reactivity with the serums of normal patients or biologic false positive reactors The RPCF has the advantage of inexpensiveness of the antigen as well as simplicity of performance and suitability for mass testing

► [This and previous reports indicate that the Reiter protein complement fixation test is highly specific and sufficiently inexpensive and technically simple as to be practical It is interesting to reflect that what started with Robert Nelson s outstanding contributions to the serologic *study of syphilis* such as the treponema immobilization test and the immune adherence phenomenon has brought the *development* of a highly specific test which utilizes a conventional serologic *technic* and an antigen derived from a strain of cultured spirochetes which has been available for many years! —Eds]

A Lipopolysaccharide Antigen of Reiter s Treponema was demonstrated and its properties were studied by G D Alessandro and C Del Carpio[8] (Univ of Palermo) The process of preparation was based on treatment of a cultured Reiter strain of Treponema pallidum with sodium desoxycholate (Portnoy and Magnuson) subsequent extraction with trichloracetic acid and precipitation of the antigen with ethyl alcohol The lyophilized antigen dissolved in 0 85% sodium chloride (1 mg /ml) resulted in an opalescent solution and had in vitro and in vivo antigenic power

(7) A M A Arch Dermat 78 181 185 August 1958
(8) Minerva dermat 33 211 215 May 1958

The lipopolysaccharide antigen elicits in animal the formation of antibodies, immune serums of rabbits repeatedly inoculated with lipopolysaccharide reacted to the homologous antigen Serums of rabbits infected with virulent T pallidum (Nichols strain) reacted to cardiolipin Reiter protein antigen and Reiter lipopolysaccharide antigen Of 25 serums of rabbits infected with the same strain all reacted to complement fixation with lipopolysaccharide antigen The chemotherapy of syphilitic rabbits besides causing disappearance of antibodies to cardiolipin and treponeme protein antigen leads to a negative reaction to the lipopolysaccharide antigen

Antipolysaccharide serum showed a marked positivity to the homologous antigen but did not react to cardiolipin or Reiter protein antigen This antiserum was positive however with suspension of treponemes Negative reaction to the lipopolysaccharide of Salmonella typhi conformed to the specificities of bacterial lipopolysaccharide antigens The lipopolysaccharide antigen was tested with various immune serums obtained from rabbits and guinea pigs by inoculation of Reiter protein antigen The results were negative or insignificantly positive and the authors infer that in the preparation of Reiter protein antigen the lipopolysaccharide antigen is not present or if present in small traces only

Of 85 serums from patients with latent syphilis positive to standard tests and to the Nelson and Mayer immobilization test 76 were positive to complement fixation with the new antigen The serum of 10 patients with latent syphilis positive to the immobilization reaction and negative to complement fixation with cardiolipin and Reiter protein antigen did not react to the new antigen The serum of 6 patients without a history of syphilis negative to the immobilization test, very likely biologic false positive gave positive reaction to complement fixation with cardiolipin and to Kahn s test but negative to complement fixation with Reiter protein antigen and with the new antigen

Tentative studies are in progress to isolate the lipopolysaccharide antigen from virulent T pallidum

Common Contagious *Genitourinary Diseases with Reference* to Ito Reenstierna and Frei Tests In about 200 patients with penile lesions seen aboard a troop ship in the Pacific zone, Donald E Tyler[9] (Rochester Minn) found only 15

(9) Brit J Ven Dis 33 278 241 December 195

with lesions or buboes characteristic of chancroid and positive reactions to the Ito Reenstierna test Of 142 men with penile lesions that did not appear to be chancroid 7 had reaction to the test Only 5 of more than 100 who had had penile lesions in the past (nearly all diagnosed as chancroid) had reactions Thus it appears that the incidence of chancroid with that of other penile lesions in the Pacific zone is probably less than 15% In the patients with penile lesions only 1 Frei reaction was observed and only a few had primary syphilitic lesions

Most of the nonsyphilitic penile lesions associated with negative Frei and Ito Reenstierna tests had been diagnosed by other physicians as chancroid but most more nearly resembled herpes genitalis Herpetiform lesions are apparently not specific for herpes simplex and studies of smears from many lesions suggested the possibility of other etiologic factors

The commonly seen simple penile lesions and the urethritides affect the Ito Reenstierna test similarly namely a light effect similar in degree to the nonspecific effects produced by immunization procedures against smallpox cholera and typhus Other similarities in these two diseases are the incubation periods appearance of the ulcers recurrent nature purported causes of recurrence not uncommon coexistence and association of chronic external penile lesions as well as chronic urethritis with Reiter s syndrome

Herpetiform penile lesions and urethral discharges in young men are apparently caused by organisms transmitted by sexual intercourse Because the etiologic agents of so few apparently infectious lesions of the mucous membranes have been determined or can readily be isolated a new concept of venereal disease is proposed based on the contagious nature of genitourinary infections rather than on whether or not intercourse is the usual mode of transmission of a particular organism Because the term venereal disease is emotionally associated with moral values it is suggested that knowledge of these diseases will be facilitated by deleting the term from the medical literature and substituting the term contagious genitourinary diseases for all transmissible genitourinary diseases whether or not the specific cause is known

► [It is of course possible that other micro-organisms could cause lesions which look like herpes simplex However if the author wants to show that in his case material the penile lesions were due to other micro

organisms he either has to demonstrate such organisms or at least show that herpes simplex virus was absent —Eds]

Group Specificity of Psittacosis Lymphogranuloma Venereum Group Skin Test Antigens in Lymphogranuloma Venereum Patients Maurice R Hilleman Aston B Greaves and Jacqueline H Werner[1] (Washington D C) carried out skin test titrations of antigens prepared from phenol treated suspensions of yolk sacs of embryonated eggs infected with lymphogranuloma venereum meningopneumonitis ornithosis feline pneumonitis psittacosis and mouse pneumonitis in serologically proved lymphogranuloma venereum patients For assay 0 1 ml lymphogranuloma venereum antigen containing 0 1, 0 2 0 4, 0 8 1 6 or 3 2 complement fixing antigen units was injected intradermally on the volar surface of one arm and the same number of units of a heterologous antigen were injected intradermally in the other arm of a patient Normal control antigen in greater concentration of yolk sac than that of the viral antigens was also given

The various psittacosis lymphogranuloma venereum group antigens tested were remarkably group specific in that all six induced a positive reaction in the lymphogranuloma venereum patients The amount of lymphogranuloma venereum antigen needed to give a positive test was extremely small usually 0 1 complement fixing unit or less The heterologous psittacosis and mouse pneumonitis antigens proved as active as the lymphogranuloma venereum antigen but the other antigens in most instances proved less active The antigenic differences between strains were so minor as to be of no practical consequence in attempts to obtain a species specific diagnosis in patients Instead the findings showed that any of the six antigens properly standardized may be satisfactory for diagnosis of lymphogranuloma venereum in man

It may be advantageous therefore to substitute a train of virus nonpathogenic for man e g feline or mouse pneumonitis virus for the highly virulent lymphogranuloma venereum virus currently used for commercial production of skin test antigen This would reduce the hazard of infection of laboratory workers handling the infectious material and improve the safety of the product for the recipient

► [Obviously false positive skin tests for lymphogranuloma venereum can be elicited in patients who have had meningopneumonitis ornithosis and psittacosis —Eds]

(1) J Lab & Clin Med 52 53 57 July 1958

Detection of Radiation Effects on Hair Roots of Human Scalp Eugene J Van Scott and Richard P Reinertson* (Nat l Inst of Health) examined microscopically the roots of hairs pulled from the irradiated scalps of patients receiving epilating and subepilating doses of ionizing radiation The types of radiation used were (1) x rays 2 Mev half value layer 12 cm Cu (2) x rays 100 kv half value layer 0 93 mm Al and (3) high energy electrons 2 1 Mev

Changes in the hair root as a result of direct ionizing radiation were detected on the 4th day after exposure and were confined to anagen (growing) hairs The earliest sign of the radiation effect was reduction in diameter of the hair bulb The matrix of the bulb when present showed the most marked decrease The internal root sheath of the hair bulb appeared thinner and contained dispersed pigment granules

After the 4th postirradiation day the entire hair bulb showed progressive atrophy leaving finally only a thin strand of tissue lying below the keratogenous zone The internal root sheath of the irradiated hair persisted and appeared thicker than normal because of the decreased diameter of the bulb remnant which it encased

At 2 3 weeks after exposure hairs with tapered shafts and small keratinized bulbs were found The keratogenous zone was absent and complete cessation of growth was apparent Other hairs that retained the keratogenous zone and evidently produced hair shafts could be found but the shafts produced were markedly thinned

The number of hairs showing alterations was proportionate to the dose of radiation sustained by the hair roots and to the interval following irradiation X radiation and electron radiation produced the same morphologic damage in the hair roots The dose of electron radiation delivered to the level of the hair roots was decreased in patients with increased thickness of hair overlying the scalp and in such patients fewer damaged roots were found

Growing Hair Roots of Human Scalp and Morphologic Changes Therein following Amethopterin Therapy The

* [illegible] Dermat 23 [illegible] September 195[illegible]

hair roots of man as in most animals cyclically pass through periods when hair is actively produced (anagen) and periods of total mitotic quiescence (*telogen*) *Roots of hairs pulled* from the human scalp may be identified as either anagen or telogen when viewed microscopically with transmitted light An actively growing (anagen) root is characterized by a dark appearing keratogenous zone immediately distal to the hair bulb melanin pigment is usually seen in the matrix of the bulb The internal and external root sheaths may be present and intact partially present or absent A resting (telogen) root has no keratogenous zone and usually has no melanin pigment Though the resting root has no internal or external root sheath its club shaped keratinized tip is surrounded by an epithelial sac Hair roots in transition from anagen to telogen (catagen) can be identified as they have internal and external root sheaths and a keratinizing bulb

Eugene J Van Scott Richard P Reinertson and Robert Steinmuller[3] (Nat l Inst of Health) examined microscopically large numbers of roots of manually extracted scalp hairs of 16 healthy adults The proportion of growing hairs was 63 96% The proportion of growing hairs of 24 patients with neoplastic diseases aged 4 89 was 24 98%

In patients given amethopterin anagen hair bulbs were *found to become atrophic and temporarily produced* a hair shaft markedly diminished in diameter The bulb recovered promptly after cessation of therapy and again produced a hair shaft of normal diameter This resulted in focal constriction of the hair shaft The morphologic changes in the roots and shafts of scalp hairs appeared in the absence of or before clinically evident spontaneous loss of hair The changes were more severe with higher doses of amethopterin Progressive atrophy of the hair bulb as may be seen following ionizing radiation did not occur Hair loss resulting from amethopterin occurs therefore by breaking off of the hair at a site of constriction in the hair shaft and not by falling out at the roots

The presence and magnitude of the changes associated with amethopterin therapy might be used to differentiate between toxicity due to disease and that due to drug particularly in patients with leukemia in whom difficulties in making this differentiation are frequently met

(3) J Invest Dermat 29 197 04 September 1957

► [These very careful studies by Van Scott and co workers of hair root changes produced as a result of various stimuli have demonstrated that these readily accessible structures of man can be a source of useful information This work and work currently being done by others are increasing the potential diagnostic usefulness of a few hairs which may be pulled easily from the scalp at the time of a patient s office visit—Eds]

Mammary Gland of Guinea Pig and Its Use as Biologic Test in Dermatologic Radiation Therapy were studied in a series of experiments reported by M Golay[4] (Univ of Geneva) Daily application to the nipple of a drop of Hormoestrol (50 µg /cc) for 15 days produces mammary gland development in the male guinea pig These proliferating mammary glands are extremely rich in mitoses easily demonstrated by the Dustin reaction produced by injection of colchicine (50 µg /100 Gm body weight) 9 hours before excision of the gland

Five days after cessation of Hormoestrol treatment the mammary gland has already begun to regress and pyknotic mitoses are definitely diminished After 15 days almost no mitoses are found and after 45 days the gland has practically disappeared reduced merely to its ducts

In mammary gland developed by 15 daily applications of Hormoestrol to the nipples an x ray dose of 400 r at 70 50 and 43 kv reduced the number of mitoses in all guinea pigs The mammary gland is about 2 5 mm from the surface where dosage at these voltages is at least 75% or 300 r If radiation of 29 kv is used the dose at 2 5 mm depth is not over 50% of the surface dose or 200 r This dose reduced the Dustin reaction in 3 of 5 animals A dose of 600 r (70 kv 0 5 mm Al filter) to a mammary gland stimulated by applications of Hormoestrol greatly reduced the number of mitoses when compared with the nonirradiated side in the same animal 1 day after irradiation but 15 days afterward there was no appreciable difference i e x rays apparently did not delay or accelerate the glandular involution A dose of 2000 r (50 kv 1 mm Al) given before daily applications of Hormoestrol did not affect development of the mammary gland and microscopically the pyknotic mitoses were the same on the irradiated and nonirradiated sides

In guinea pigs whose mammary glands had been stimulated by 15 applications of Hormoestrol petrolatum containing 20% podophyllin which was applied to the left mam

(4) Dermatologica 117 81 September 1958

mary region for 4 hours produced no effect on the mamm glands

Nipple Test and Recuperation of Mitotic Capacity af Irradiation M Golay (Univ of Geneva) administe x ray doses of 400 800 and 1 600 r (70 kv 5 ma 0 5 mm filtration 24 cm focus skin distance) to the left nipple male guinea pigs At varying intervals a single applicat of Hormoestrol (50 µg/cc) was made to both nipp with injection of colchicine 24 hours later followed n hours by excision of both nipples

With a dose of 400 r it was generally observed that af 2 days the mitotic power had not reappeared and that Dustin reaction was greatly diminished After 5 days mitotic capacity had reappeared and there was no appre able difference between the two nipples With 800 r usua after 10 days the mitotic capacity had not reappeared, after 15 days there was no difference between the two sid With 1 600 r, the mitotic capacity had not reappeared af 15 days but was equal to that on the nonirradiated side in days

These experiments show a relation between radiation do and time required for recuperation of mitosis i e the ti is lengthened with increased dosage In other experimen one nipple was irradiated with 2 doses of 400 r administer 1 month apart Five days after the second irradiation t Dustin reaction was reduced in 2 of 4 guinea pigs suggesti that the epidermis of the irradiated nipple remembered t dosage of 400 r received a month earlier

Effect of X rays on Epidermal Mitoses in Human Cond loma Acuminatum was studied by M Golay[6] (Univ of G neva) in 3 patients A dose of 400 r (70 kv 0 5 mm Al filte was used since this is the amount which depresses t Dustin reaction in the epidermis of the nipple and mamma gland of male guinea pigs stimulated by Hormoestrol Im mediately after selected condylomas of the patients were i radiated, petrolatum containing 20% podophyllin was ap plied to both irradiated and control condyloma for 4 hour Nine hours after removal of the podophyllin ointment th irradiated and control condylomas were excised The contr lesions showed numerous pyknotic mitoses which were al sent from the irradiated lesions

(5) Dermatologica 117 17 0 September 1958
(6) Ibid pp 21 23

These findings indicate that sensitivity of human epider nal mitoses is similar to that of epithelial mitoses in the nipple and mammary gland of the guinea pig

► [An interesting and informative series of animal and human studies with x radiation These studies once more point out that while some of the information gathered from experiments in laboratory animals may have application in man (as for example in the condyloma studies) it does not apply in all instances Certainly the findings in guinea pig breast tissue are not applicable to man since instances are known in which x radiation and gamma radiation to the developing breast tissue of the human female has distinctly altered and retarded the development of the glandular elements —Eds]

Effect of Preirradiation Intraperitoneal Injection of Cysteamine upon Skin and Depilatory Reactions Produced by X rays in Legs of Mice was investigated by C W Wilson (Westminster Hosp London)

PROCEDURE.—The left hind legs of 11 6-week old mice were given 2 000 r generated at 200 kv Immediately afterward the animals were given an intraperitoneal injection of cysteamine 3 mg /20 Gm Then the right hind legs were irradiated similarly to the left legs Frequent examinations were made for 28 days for any effects produced on the hair and skin of the irradiated areas

Intraperitoneal cysteamine injection just before local irradiation afforded considerable protection against the skin and depilatory effects of the x rays Epilation was less complete and skin reactions much less severe in the legs irradiated after administration of cysteamine The observations seem to confirm the belief that the primary protective action of cysteamine occurs at the cellular level

► [This and other compounds have been shown to increase tissue tolerance to various forms of ionizing radiation The truly practical aspects of findings such as these have yet to be demonstrated in man While the goal is to find some means of increasing whole body tolerance to radiation it would be interesting to know if protective chemicals will allow normal tissue to effectively withstand greater doses of radiation in treatment of malignant growths —Eds]

Comparison between Visual Grading and Reflectance Measurements of Erythema Produced by Sunlight In devising methods of skin color measurement for verbal descriptions or rating scale it is desirable to contrive methods which provide parallel columns of 2 or 3 digit numbers for evaluation by standard statistical methods The photoelectric reflectance meter with appropriate filters and standard appears to meet this desideratum Two general types of use of the reflectance meter in evaluating skin color are evident The first is expression of color as tristimulus co ordi

(7) Brit. J R di 1 31 100 101 Febru ry 19 8

nates for purposes of specifying skin color in terms that can be compared with ointments cosmetics prostheses and perhaps matching of recipient and donor sites in skin grafting The other general approach is to measure melanin and hemoglobin independently and thus quantitate pigmentation in the presence of erythema or evaluate the degree of erythema in patients with different basic skin colors

Farrington Daniels Jr and J Donald Imbrie[8] (Univ of Oregon) studied 75 subjects whose backs were exposed to sunshine for 10 120 minutes A total of 1 865 sets of observations were made These observations included the visual grading of erythema and melanin pigmentation (tan) on a scale of 0 5+ and the making of reflectance measurements through red blue green and amber tristimulus filters Comparison between the two types of observations was made and the four glass filters were compared to narrow band interference filters

Studies to date suggest that an interference filter with a transmission maximum at about 542 576 mμ should be used to provide a system maximally responsive to erythema Either an interference filter with transmittance maximum between 620 and 660 mμ or a red glass filter (such as Corning glass no 2403) should be used to measure melanin independently of erythema though some effect from oxyhemoglobin and reduced hemoglobin cannot be avoided

► [Among the most needed of mechanical devices in dermatology is one which will read and grade in a simple way the erythema and the pigmentation produced in human skin by external agents including various forms of radiation —Eds]

Benzophenones Ultraviolet Light Absorbing Agents Benzophenones are currently used industrially to protect objects and materials that are subject to discoloration or deterioration from exposure to ultraviolet radiation John M Knox Jere Guin and Earl G Cockerell[9] (Houston) investigated their usefulness in dermatologic vehicles as topical sun screening preparations Benzophenones were incorporated into 95% ethanol and vanishing cream and compared in different concentrations to tannic acid para aminobenzoic acid (PABA) and currently used commercial sun screens and sun tanning products

The minimal erythema dose of ultraviolet light for white

(8) J Invest Dermat 30 295 304 June 1958
(9) Ibid 9 435-444 December 1957

albino rabbits under the experimental conditions was 25 30 econd This was unchanged by the application of ethanol and was 55-60 seconds when vanishing cream base was applied Tannic acid PABA 2 4-dihydroxybenzophenone and 3 benzoyl-4 hydroxy-6-methoxy benzenesulfonic acid were all effective ultraviolet light absorbers in 10% concentration but PABA and 3 benzoyl-4 hydroxy 6-methoxy benzenesulfonic acid were the most effective With the latter agent the minimal erythema dose was increased to more than an hour Concentrations of 5% of the various light absorbing agents were less effective than 10% concentrations The best protection provided by any of the 24 commercial preparations tested was 3 5 minutes and only 4 products gave such satisfactory results

Because 2 4-dihydroxybenzophenone is insoluble in water and is almost colorless this benzophenone in an alcohol and silicone oil vehicle was chosen for clinical studies This formulation appeared to provide excellent protection for photosensitive persons fishermen and sunbathers

Absorption of Antimalarial Drugs in Human Skin Spectroscopic and Chemical Analysis in Epidermis and Corium Bertram Shaffer Milton M Cahn and Edwin J Levy[1] (Univ of Pennsylvania) determined the concentration of some antimalarials (quinacrine chloroquine hydroxychloroquine and amodiaquin) in separated epidermis and corium of normal persons who had ingested these drugs Quinacrine dihydrochloride (Atabrine*) was taken in doses of 100 mg 3 times a day for a week then 100 mg a day for 3 weeks The dose of chloroquine diphosphate (Aralen*) was 250 mg twice a day for 1 week then 250 mg a day for 3 weeks Both hydroxychloroquine sulfate (Plaquenil*) and amodiaquin hydrochloride (Camoquin*) were taken in doses of 200 mg twice a day for a week then 200 mg daily for 3 weeks

All specimens showed a higher concentration of the drug in the epidermis than in the corium The epidermis dermis ratio was about 5 1 for chloroquine 10 1 for quinacrine and 1 1 or greater for hydroxychloroquine and amodiaquin Drug concentration in the epidermis ranged from an average low of 19 2 μg /Gm for quinacrine to an average high of 31 6 μg /Gm for amodiaquin Epidermal concentration of antimalarials is believed to result largely from the greater af

(1) J I t D rm t 30 341 345 J 1958

finity of these agents for epidermal protein than for that of the corium although relative desiccation of the epidermis may play a partial role

Ultraviolet absorption curves of normal human separated epidermis and corium and similar absorption curves for tissue from the volunteers who had ingested antimalarial indicated that these drugs had no perceptible absorption effects so far as the ultraviolet spectrum was concerned, on either epidermis or corium Superimposed absorption curves of the antimalarials indicate that their principal absorption band occur at different points in the spectrum and that these do not correspond to the normal sunburn spectrum range This would indicate that the antimalarials play little or no role in modifying the normal absorption of ultraviolet light by epidermis so far as sunburn or polymorphous light eruption is concerned The data further tend to substantiate the thesis that the action of these drugs in suppressing the manifestations of polymorphous light eruption is other than that of an intraepidermal sunscreen

► [The marked differences in the concentrations of these antimalarial in the epidermis as compared to the dermis were noted within the 4 weeks after the start of the drug It would be interesting to learn whether the concentration of these compounds was equal throughout the epidermis or was greater in some of the cell layers than in others If spectrophotometric examination of single or a few cells is feasible then this method of tagging the epidermal cells with selected antimalarial drugs might be used as a means of studying the life cycle of epidermal cells —Eds]

Evaluation of Level of Properdin in Normal Adult Humans and in Certain Disease States Preliminary Report is presented by Victor D Newcomer Earl G McNall Carlyn Halde Edwin T Wright and Thomas H Sternberg (Los Angeles) The properdin levels of apparently healthy male and female Caucasians aged 20 85 were determined to establish normal values A correlation between age and properdin level was observed About 90% of the levels of properdin in the serum of subjects aged 20 40 were 67 184 units/ml serum In subjects aged 71 85 about 90 of the serum properdin level were between 17 and 84 units Subjects aged 40 60 had properdin levels averaging lower than those in the younger group and higher than those in the older group No relation between properdin level and sex was detected The concentration of properdin in a large number of Negroes was low compared to levels of Caucasian of similar ages

(2) J Invest Dermat 30 233 236 May 1958

The levels of properdin in patients with carcinomatosis pemphigus lupus erythematosus herpes zoster diabetes mellitus and atopic dermatitis were studied by single determinations Some patients with herpes zoster lupus erythematosus and pemphigus had levels lower than those considered normal for the corresponding age groups Serial determinations and study of more cases will be necessary to clarify these findings

Significance of Redox Potentials in Physiology and Pathology of Skin According to H Langhof[3] (Univ of Greifswald) oxygen consumption of the skin consisting of 0 8 cu mm/hour/mg dry substance is extremely low as compared for example with that of the kidney tissues (25 cu mm) Their energy metabolism occurs according to the Szent Gyorgyi system of biologic respiration

Many dermatoses are caused by disturbances in the ferment metabolism of the skin The reduction ability of the germinative layer is determined mainly by the skin sulfhydryl which contains the redox systems cysteine cystine reduced glutathione oxide glutathione thioglycollic acid and thiolenzymes The ferments in the skin (hexokinase carboxylase succinodehydrogenase and kathepsin) are thiolferments that are activated by certain reductors and inactivated by oxidative agents Hexokinase which is located at the cell membrane is closely related to the glucose assimilation of the cell Interruption of the glucose assimilation by restraining hexokinase starts keratinization in the stratum granulosum The keratinization goes through these stages (1) stretching of colloidal dispersed cell protein to polypeptide threads (2) combining of these parallel running protein myceliums through disulfide bridges and salt compounds between COOH and NH groups and (3) loss of swelling and shrinkage of the cell plasma dissolution of nuclei and mitochondria of the *epidermis* cell

In psoriasis normal withering of the epidermal cells is restrained by abnormally high concentration of reducing agent in the upper epidermal layers Psoriatic parakeratosis can be provoked by reducing agents and checked by oxidative agents Oxidative agents in high doses restrain the energy metabolism of the germinative layer of the normal skin by blocking the sulfhydryl containing ferment system This

3 A h kl ... D rm 20 445 8 39 8

leads to a dysenzymatic hypoxidosis' Chronic arsenic poisoning with hyperkeratosis melanosis and light sensitivity is an example of the skin syndrome caused by activation of the skin redox *potential The similar response of the skin* after prolonged exposure to ACTH heavy metal tar and pitch by hyperkeratosis hyperpigmentation and susceptibility to infection is interpreted as activation of the germinative *layer by oxidative agents* Absence of reducing substances such as vitamins A C and B complex may have the same effect on the metabolism of the epidermis as has been noted in vitamin deficiency dermatoses such as pellagra or melano keratosis scorbutica

Histamine Levels in Human Skin were investigated by Herbert H Johnson Jr[4] (Western Reserve Univ) All determinations were made within 24 hours in 13 cases of traumatic sudden death 12 by automobile accidents and 1 from a traumatic air embolism Earlier guinea pig experiments had shown that this interval did not alter skin levels significantly

Marked variations in human skin histamine levels were found in different regions of the body The highest levels were on the upper lip and eyelid with decreasing levels in the submental triangle scalp infraclavicular region lower abdomen and skin over the xiphoid cartilage In the scalp the average level (11 determinations) was 21 5 µg/Gm infraclavicular region (11 determinations) 8 2 µg/Gm lower abdomen (12 determinations) 7 6 µg/Gm and over xiphoid cartilage (10 determinations) 6 6 µg/Gm Too few determinations could be made in other areas to establish average levels

On the basis of experiments with the pharmacologic method of histamine determination Halpern and associate have proposed the hypothesis that histamine exists in tissue in three forms (1) free histamine present in only minute quantities in body fluids (2) labile histamine present normally in a physiologically inactive form releasable in a few minutes by a pathologic process such as that induced by histamine release substances and (3) combined histamine released by acid hydrolysis technics of extraction which determine both the labile and combined histamine simultaneously

Using the microchemical method of histamine determina

(4) A M A Arch Dermat 76 726 730 December 195

tion Johnson obtained a three fold increase in histamine levels of human abdominal skin by acid hydrolysis These findings tend to confirm the Halpern hypothesis

Histamine levels determined by the microchemical method in this study were comparable to pharmacologically determined levels reported in the literature The latter levels also were found to increase markedly when acid hydrolysis methods were used

Assay of Causes of Allergies by Histamine Fixation Evaluation of Results in Various Dermatoses are presented by J Tappeiner H Tirschek and P Wodniansky[5] (Univ of Vienna) The serum of healthy persons contains gamma globulin which in vitro inactivate 20-40% histamine They determine according to Parrot and his associate the so called histamine fixation capacity or histaminopexy of the serum In allergic persons this histamine inactivating ability is partly or completely absent Lack of histamine fixation is an almost constant characteristic of the allergic patient but not of the healthy person Histamine fixation is independent of clinical allergic manifestations and persists after the skin changes have subsided

The authors assayed histamine fixation to clarify the possible allergic background in various skin diseases They confirm Parrot s contention that histamine inactivating ability is decreased or absent in allergic diseases

The number of patients with dermatoses of uncertain cause was too small to reach definite conclusions concerning the allergic or nonallergic cause An allergic background could be suspected in essential generalized pruritus and in idiopathic erythema exudativum but not in psoriasis vulgaris

Variations in Histamine Fixing Capacity of Blood Serum in Course of Eczema in Adults may be used as a measure of the allergic terrain since it is absent or greatly decreased in allergic persons Edwin Sidi A Reinberg M Hincky and J Bourgeois Spinasse[6] (Paris) examined 122 patients from this point of view *In* 75 (35 women) with atopic eczema 7 showed no histaminopexic power and 11 showed a slight reaction thus this function was disturbed in 67 or about 90 The proportion was essentially the same in 47 patients

(5) Arch kl pe D m t 07 261 67 1958
(6) P se m d 66 343 345 F b 26 1958

(23 women) with contact eczema of whom 32 showed absence of histaminopexic capacity and 7 had values decreased to 10% (normal 30%) With clinical improvement histamine fixation of serum was 15% or over in 17 of 25 patients with contact eczema and in 28 of 46 with atopic eczema In the latter group histamine fixation increased in 30 patients remained unchanged in 13 and decreased in 3 Of those showing improvement of contact eczema histamine fixation increased in 17 was unchanged in 5 and decreased in 1 In general the capacity for histamine fixation is increased with clinical improvement, but there is no strict correlation between degree of improvement and histaminopexic increase

This correlation suggests the possibility of treatment aimed at modification of the allergic terrain by (1) correction of metabolic disorders (spasmophilia hypothyroidism imbalance in protein lipid metabolism), (2) use of nonspecific corticoids and (3) injections of human serum with high potency for histamine fixation This treatment produced improvement in about one third (19 of 55) of the patients in whom it was tried In about one third of those with contact eczema recurrences were less severe and of shorter duration after serum therapy In some patients with atopic eczema dosage of cortisone could be reduced or discontinued after treatment with histaminopexic serum this effect was most marked in 4 patients aged 60 75 Exacerbations of eczema or other allergic manifestations occurred in 3 instances (among over 100 serum injections) Similar reactions have been reported with serum injections for asthma Although in most cases improvement in eczema is accompanied by improvement in other allergic symptoms (rhinitis asthma or urticaria) in 5 patients (2 adolescent) the asthma increased after the eczema improved

The authors conclude that the histamine fixing capacity of blood serum constitutes a valuable means of following the clinical course of eczema of determining the effectiveness of therapy and of predicting recurrence Treatment with serum of high histaminopexic potency is worthy of trial particularly in patients in whom the histaminopexic capacity is decreased or absent

► [Under the circumstances it may be difficult to a e the therapeutic effects of injection of human serums with high potency for histamine fixation In patients with atopic dermatitis it is the rule rather than the exception that the dose of corticosteroids can be reduced gradually And in

contact dermatitis it may be impossible to be certain that recurrences are less severe and of shorter duration unles the patient is repeatedly and deliberately re-exposed to known quantities of the causal agent —Eds]

Pruritus and Proteolytic Enzymes Samuel Monash and J Frederick Woessner Jr[7] (Miami) report that the proteolytic enzymes ficin papain pancreatin and chymotrypsin when tested by scratch testing in a concentration of 1 10 to 1 100 in buffer solution produce pruritus diminishing in intensity in the order given The pruritogenic character of the enzymes ficin papain and pancreatin is not lost when their proteolytic activity is destroyed by heating dry at high temperatures or by boiling The pruritogenic activity of a 1 1000 concentration of lyophilized trypsin in isotonic saline is still present even though the dry enzyme is inactivated by heating at 140 C for 2 hours Of 9 persons tested with intracutaneous injections of unheated trypsin solution 5 reacted with itching lasting 2½ 5 minutes Four of the 5 reactors also received injections with heated trypsin solution and all reacted with itching lasting 2-4 minutes

When Mucuna pruriens spicules were rubbed back and forth on a small area of the skin of the forearm itching was produced consistently The spicules did not lose their pruritogenic character when heated dry at temperatures high enough to destroy their proteolytic capacity The enzyme is very resistant to heat requiring 1½ hours at 140 C for complete inactivation After prolonged exposure to moisture the spicule were no longer pruritogenic though this procedure did not destroy their enzymatic activity

These studies fail to show a parallelism between the proteolytic and pruritogenic activity of the enzymes and the findings do not support the theory that there is a causal relation between the two

► [The results reported by Monash and Woessner are not in agreement with those of the original work of Shelley and Arthur Shelley (personal communication) among other comments stated that Monash and Woessner used such high concentrations of proteinase that the pruritus produced could be the result of a nonspecific foreign protein effect rather than a specific proteinase action We look forward to a clarification of the difference in the findings of these investigators – Eds]

Distribution and Behavior of Cutaneous Nerves in Normal and Abnormal Skin The recently introduced method of in vivo staining of nerve fibers by hyaluronidase and methylene blue has proved dependable for identifying cutane

(7) A M A Arch Derm 78 214-217 August 1958

ous nerves and Koelle's histochemical staining technic has permitted visualization of deposits of acetylcholinesterase (the specific enzyme) and nonspecific cholinesterase A Scott[8] (St Bartholomew's Hosp London) used these technics in the study of cutaneous innervation in 31 subjects with normal skin, 10 with normal skin which had been exposed to an erythema producing physical agent (ultraviolet thorium X or grenz radiation) 10 normal subjects in whom small areas of skin had been exposed for 2 minutes to cold or heat and 10 patients with psoriasis 53 with eczema 31 with atopic dermatitis and 14 with urticaria Of the patients with urticaria 8 presented the clinical criteria ordinarily accepted for diagnosis of cholinogenic urticaria Intradermal tests were carried out in a number of these subjects using acetyl choline (1 10 000 in saline) histamine (1 100 000) atropine (1 1000) nicotine (1 10 000) prostigmine (1 10 000) and Trafuril® cream (thurfyl nicotinate 5%) The first five materials were administered by injection in 0 1 ml doses Trafuril® was locally applied

It was found that sensory nerve terminations in the trunk and limbs were represented not as specialized end organs but by fibrils ending freely in the superficial dermis the deeper epidermis and about the hair follicles Sensory discrimination thus depends on functional impulse variations in the nerve fiber or central neuron identification

Specific acetylcholinesterase was identified in sensory fibers but appeared to be concerned not with sensory impulse transmission but with the passage of antidromic impulses concerned in axon reflexes induced by mechanical (stroking) physical (ultraviolet rays) or chemical (histamine etc) means The presence of this enzyme appears to be related directly to the production of erythema but is not necessarily causally concerned in transmission of the nerve stimuli

Motor autonomic nerves arborize about all the sweat glands Normally only those nerves supplying the eccrine glands contain free acetylcholinesterase In only one state —cholinogenic urticaria—did the apocrine gland nerve supply contain this enzyme

Nerves terminating about the pilomotor apparatus did not contain acetylcholinesterase No nerve fibers ended within

(8) Brit J Dermat 0 1 1 Janu y 1958

the substance of the arteriolar walls but sensory nerve terminals were adjacent to most of them Usually only occasional small arterioles contained specific acetylcholinesterase in the walls but in the presence of erythema this enzyme was present in all the arteriolar walls and at the ends of the adjacent sensory nerves It appeared that the acetylcholinesterase reached the vessels by diffusion through tissue

Nonspecific cholinesterase was present in occasional basal epidermal cells of normal skin but in all the basal cells affected by irradiation eczematization Trafuril® and urticaria Psoriatic lesions were unique in that the entire epidermis contained cholinesterase deposits

The structural form of the cutaneous nerves was not disturbed by any of the tests used or in any of the dermatoses studied

In general the skin followed the pattern of Lewis s triple response in its reactions to test materials This reaction consisted of a central wheal (with an injection) and a surrounding vasodilatation with visible erythema associated with the appearance of free acetylcholinesterase in the sensory nerves and the small arterioles The use of acetylcholine demonstrated a minor variation in that this substance had a direct effect on the vessels as well as an indirect one via the usually involved axon reflex Mainly these tests provide a means of determining the integrity of the local axon reflex the responsiveness of the local vasculature and the degree of permeability of the tissue tested

Abnormal test reactions were elicited in postradiation skin eczematization and atopy In the first two conditions the normal response was obtained only with acetylcholine The variation from normal in the other tests appeared to be due to lack of response of small arterioles The alterations observed in the responses in atopic dermatitis were due to the presence of tissue edema and could be prevented by use of hyaluronidase

Though no conclusion can be reached with regard to the basic disorder in atopy an excess of bound acetylcholine in the vessel wall may so depress synthesis of this material that *arteriolar* constriction results with altered vascular permeability

► [Among] the interesting findings in this study are the altered responses in atopic dermatitis which Scott explains on the basis of tissue edema (see also article by Davis and Lawler this YEAR BOOK p 155) and the

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(8) Brit J Derm [illegible] January 19[illegible]

Effect of Dermabrasion on Fingerprints Preliminary Report describing results in 2 cases is presented by James W Burks Jr[1] (Tulane Univ)

Man 53 was treated for arsenical keratoses The volar surface of the distal phalanx of the right 5th finger which contained a keratotic lesion was subjected to dermabrasion The area was planed with a Kurtin wire brush to a depth at which minute herniations of yellow fat appeared An antibiotic absorbable gelatin powder and Telfa non adherent strips were applied daily for 4 days after which only Telfa gauze was used as a dressing

On the 23d day after planing the crust was easily removed The underlying skin was pink did not have the appearance of a scar and was devoid of epidermal ridges On examination of the area with a hand lens the normal arrangement of whorls was seen to be replaced by minute thin crisscrossed and parallel linear markings similar to those on the dorsal surface of the web between the thumb and index finger

The patient observed no difference between planed and unplaned fingers insofar as appearance motion or reactions to heat and cold were concerned but noted more acute sensitivity to touch in the planed finger Identification experts considered the postplaning fingerprints worthless in establishing the identity of the subject

The basic dermatoglyphic configurations of volar skin have heretofore been considered permanent and have been used as unalterable and unduplicative means of identification This report which describes the alteration of these patterns by dermabrasion vitiates the principle of finger printing and therefore has important medicolegal implications The services of a dermatologist may be sought by the criminal in an attempt to efface fingerprints and the dermatologist must guard against the hazard of abetting such criminals

► [The findings of Plotnick and Pinkus (see the following article) indicate that even after the epidermis has been removed the fingerprint characteristics of the individual still are discernible in a double line pattern in the cutis It appears likely that the dermabrasion as performed by Burks destroyed these dermal double ridges —Eds]

Epidermal vs Dermal Fingerprint Experimental and Anatomic Study is reported by Harold Plotnick and Hermann Pinkus (Detroit) Fingerprint experts hold that the dermal print is of considerable practical importance in establishing the identity of bodies when the epidermis has been altered by such processes as maceration desiccation mummification or putrefaction The dermal print though finer and less clearcut than the epidermal possesses the same ridge

(1) A M A Arch Dermat 77 8 11 Jan ry 1958
( ) Ibid pp 12-17

presence of acetylcholinesterase in the apocrine gland nerve supply only of patients with cholinogenic urticaria—Eds]

Effect of Inhibition of Nonspecific Cholinesterase on Perception of Tactile Sensation in Human Volar Skin was investigated by Harry J Hurley and George B Koelle[9] (Univ of Pennsylvania)

METHOD—Volar skin of the great toes was chosen as the test area because of the preponderance of specialized and nonspecialized nerve endings found there Perception of light touch sharp dull discrimination, pressure and pricking pain were tested Distilled water 0 02 cc was pipetted onto the volar skin of one great toe within an area 1 3 cm in diameter and 0 02 cc undiluted diisopropyl fluorophosphate was placed on a similar area on the opposite great toe Both areas were quickly capped with a small glass cup that was firmly taped to the surrounding skin Both liquids were allowed to remain on the skin for 1 hour during which time blood pressure and pulse rate were recorded every 10 minutes as a precaution against possible development of systemic intoxication After removal of the cups the treated skin was re examined for sensory perception Punch biopsy specimens were taken from 2 subjects

On removal of the glass cups grossly visible eccrine sweat droplets were evident on the skin of the treated toes of all 4 subjects studied The skin of the control toes showed no such secretion After removal of the cups no significant differences were found in sensory perception between the control and treated toes and no variation from the initial pretreatment evaluation Histochemical studies of the volar skin treated with distilled water revealed specific cholinesterase in its normal sites viz in nerve fibers about the secretory tubules of the sweat glands about the digital arteriovenous anastomoses in red blood cells and in many free endings supplying the skin Nonspecific cholinesterase was visualized in Meissner s tactile corpuscles In the treated skin there was no specific or nonspecific cholinesterase

The authors conclude that the failure to influence significantly the perception of light touch pressure and pricking pain by local inhibition of cholinesterases by diisopropyl fluorophosphate indicates that these enzymes have little or no function in the immediate processes concerned with transmission of cutaneous sensation Nonspecific cholinesterase of specialized cutaneous nerve endings possibly may serve a nutritional or trophic function and its depletion or prolonged inhibition (weeks to months) would produce marked alteration in cutaneous sensory perception

(9) J Invest Dermat. 31 243 245 October 1958

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(1) A.M.A. Arch Derm 77 8-11 J n ry 1958
(2) Ibid. pp 12-17

details as the outer surface of the epidermis. This was supported by the authors' experimental studies.

Fingerprints were made using recently amputated digits from operating rooms. Subsequently the specimens were immersed in 0.25% acetic acid solution for 72 hours to produce separation of the epidermis from the dermis. The macerated epidermis was gently peeled away with tissue forceps leaving a clean surface which represented the upper dermis. Histologic examination of such a specimen revealed complete absence of epidermis. Prints were then made of the digits from which the epidermis had been removed.

When the dermal surface was inked the imprint consisted of a double line rather than the usual single line pattern. This was because when epidermis is removed a double set of papillae for each epidermal crista remains. The dermal prints were identical with the epidermal ones in all details.

In the preparation of the specimen for dermal impression the digit must be heavily inked and rolled over the card with minimal pressure. If this is not done the double row papillary ridge pattern characteristic of the dermal print is not obtainable.

► *[The role of the dermatologist may be far reaching. This article was written after Dr. Pinkus was consulted by police authorities concerning the anatomic basis of the differences between epidermal and dermal finger prints.—Ed.]*

Studies on Epidermal Regeneration by Means of Strip Method. Murray C. Williams and Rosie Hunter[3] *(Detroit)* investigated the relative importance of loss of keratin cells and of cellular trauma due to dehydration following the stripping procedure. Covering the stripped skin with cellophane tape as an occlusive dressing to minimize dehydration caused a decreased mitotic response as compared to an uncovered stripped area. Therefore besides cellular trauma the effect of dehydration due to loss of stratum corneum appears to be one factor responsible for the mitotic response.

To study *how far the mitotic unrest spreads from* the keratin stripped epidermis, biopsy specimens were taken from apparently normal skin at the edges of the stripped site. Skin 3-6 mm from the stripped area showed an increased mitotic count which in most cases was only slightly less than that of the stripped skin. In all specimens the stratum corneum appeared to be of normal thickness, confirming the

(3) J Invest Dermat 9 407 413 December '39

clinical impression that the stratum corneum was intact in these areas Spread of mitoses may be due to minimal indirect trauma to the surrounding epidermis during keratin stripping or possibly the traumatized actively mitotic cells affect the surrounding epidermal cells by direct contiguity Another possibility is that spread of mitoses may be associated with the triple response of Lewis After stripping of an area too vigorously or applying an irritating substance to the surface of the stripped skin increased redness and slight edema occur in this area and a red flare appears around it

Studies were undertaken to demonstrate any possible change in the concentration of acid phosphatase and succinic dehydrogenase in the rapidly proliferating epidermal cells after stripping Histochemical examination revealed no change in concentration of acid phosphatase as compared to normal controls and no succinic dehydrogenase was found in the epidermal cells in normal or stripped skin

Qualitative and Quantitative Data on Melanocytes in Human Epidermis Treated with Thorium X Renato J Staricco[4] (Wayne Univ) observed the behavior of melanocytes of human skin after stimulation with weak concentrations of thorium X that did not produce marked inflammatory reaction Melanocytes reacted with increased functional activity but did not increase in number when the stimulation was mild More melanin was produced and the cytoplasm became larger and polymorphic with much longer dendrites than are seen normally The number of melanocytes seemed to decrease slightly in the 2 weeks after stimulation which was apparently due to a process of elimination Some of the melanocyte gradually moved up into the prickle cell layer granular layer and finally horny layer losing most of their dendrites in the process but retaining their vital enzymatic activity until they reached the stratum corneum The dendrite lost during migration leave amorphous and irregular masses of melanin in the intercellular spaces and between the keratin sheets No transformation of malpighian cells into melanocytes was observed

Somewhat stronger stimulation with thorium X produced a moderate increase of the number of melanocytes per square centimeter of skin surface This increase seemed to parallel the elongation of the rete ridges and the number of melano

( ) J I est Dermat 9 18 1?5 Septembe 19 7

cytes per square unit of dermoepidermal junction probably remained fairly constant

Fifteen days after the stimulus had been set the behavior of the melanocytes that did not leave the dermoepidermal junction was variable Some were small and surrounded by a vacuum clear area having the approximate shape of the melanocyte, whereas others were as large as the ones found at 7 days This difference might signify actual shrinkage whereby an extracellular accumulation of fluid is produced Or a process may be involved similar to that in amphibian melanophores in which the pigment granules may concentrate around the nucleus leaving the transparent cytoplasm and dendrites almost invisible In that case the clear area actually would be a part of the melanocyte Depending on which of these explanations is true the increased size of the melanocytes after stimulation would be either a real enlargement if the clear space seen later is extracellular or an apparent enlargement if the clear space is cytoplasm deprived of melanin

The demonstration of high level pigmented dendritic cells showing dopa oxidase and tyrosinase activity after mild stimulation with thorium X seems to support the view that melanocytes are eliminated by desquamation also under normal conditions It has been shown that the epidermis exfoliates more rapidly after small doses of thorium X This fact together with greatly increased functional activity of the melanocytes and radiation injury possibly suffered by some of them may be the reason more cells are eliminated and at a rate so rapid they still contain melanin granules and active enzymes

► [It may be worth repeating here that thorium X is a naturally occurring radioactive material of the thorium series which has been used therapeutically by dermatologists for over 45 year (Nageli O E and Jessner M Therap Monatsh *27* 765 1913) It has a half life of 3 64 days and is an alpha beta and gamma emitter Of the radiation energies produced 92% is alpha 4% beta and 4% gamma Experience has proved it to be a useful therapeutic agent among it action is that of an excellent stimulus of pigmentation in human skin With ample precaution it is safe and easy to use It is commercially available and may be used without authorization from the United State Atomic Energy Commission —Eds]

Melanocyte Distribution in Forearm Epidermis of Freckled Human Subjects as investigated by Aodan S Breathnach[5] (St Mary's Hosp Med School London) In local

(5) J Invest. Dermat 29 253 61 October 1957

zed areas of pigmentation (freckles) in the skin of 5 freckled subjects significantly fewer active melanocytes/unit area could be demonstrated in dihydroxyphenylalanine (dopa) treated material than in adjacent paler areas or in corresponding epidermal areas of 5 nonfreckled subjects The melanocytes of freckles showed characteristic signs of hyperactivity compared with those of surrounding less highly pigmented epidermis Supravital staining with methylene blue gave a strong impression that the difference in number of melanocytes present in freckles and surrounding epidermis is a real one in total numbers and not due to some of the cells of the freckle being in a completely inactive (dopa negative) condition These findings confirm conclusions of previous workers that a high degree of epidermal pigmentation depends more on the level of functional activity of the melanocytes than on the actual numbers present in a given area

Potential frecklers are nonfreckled at birth and do not appear capable of producing freckles until ages 2-4 It is not known whether such persons are born with localized areas of low melanocyte concentration at the sites of future freckles or whether the melanocytes are uniformly distributed as they apparently are in the nonfreckled If the latter is the case it is not known what influences operate to produce the subsequent uneven distribution in numbers and pigment concentration

At the edge of a freckle there is a sharp demarcation between immediately adjacent areas of epidermis with different characteristics When a freckle spreads to involve an adjoining paler epidermal area the latter must presumably take on the characteristics of the former This must involve reduction in the total number of cells in the paler area plus stepping up of the tyrosinase activity of the rest or the operation of some selective influence which leads to stepping up of the activity of some cells and suppression of that of others without at the same time affecting the total number present

Observations on Tyrosinase Activity in Melanocytes of Freckled Human Epidermis are presented by Aodan S Breathnach[6] (St Mary Hosp Med School London) Samples of normal human skin each bearing a freckle and an area of surrounding paler skin were removed from the fore

(6) J I st Dermat 30 153 155 M h 1958

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(5) J Invest Dermat 29 253 61 October 195

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(6) J I vest Dermat 30 153 158 M h 1958

arm and knee Pure epidermal sheets were obtained by tryptic digestion and these were incubated with different substrate mixtures 0 05% l tyrosine at pH 6 8 with phosphate buffer similar l tyrosine solution to 50 ml of which 0 4 ml of 1% copper sulfate solution was added buffered 0 1% solutions of l tryptophan and 5 hydroxytryptophan and 0 1% dopa

A reaction developed in the melanocytes of both freckle and paler epidermis of all specimens incubated with buffered tyrosine alone Localized variations in tyrosinase activity were observed and could be correlated with morphologic differences differences in population density of the cells concerned and with the amount of pre formed epidermal melanin In areas where melanin was most abundant melanocytes were typically large with many branches and comparatively sparse These cells exhibited a relatively high level of individual tyrosinase activity These findings based on observations of the tyrosine reaction were identical with those achieved when dopa was used as a substrate

Differences in tyrosinase activities of the melanocytes of freckles and paler epidermis were not abolished by provision of an excess of copper in the substrate medium This strongly suggests that the localization of individual freckle cannot be accounted for in terms of local differences in the concentration of epidermal sulfhydryls affecting availability of copper for the tyrosinase Certain natural features of freckling including its absence before age 2 3 and the sharp boundary between freckle and adjacent paler epidermis which lies within the territory of a single melanocyte tend to support this conclusion

Other factors such as morphologic differences between the melanocytes of freckles and pale epidermis and difference in population density must be considered in attempting to account for freckling If freckling were present from birth it would be tempting to suggest the existence in freckled epidermis of two genetically distinct types of melanocytes and that it is the location of representatives of these different types which determines the sites of freckles However since freckling is acquired postnatally this is unlikely No reaction was observed in melanocytes incubated with l tryptophan or 5 hydroxytryptophan therefore neither amino acid is a likely substrate in normal human melanogenesis

Histology and Cytochemistry of Human Skin XIII Blood Supply of Hair Follicle William Montagna and Richard A Ellis (Brown Univ) demonstrated electively the terminal capillaries in frozen section of skin by use of the azo dye technics for alkaline phosphatase Active hair follicles have a rich plexus of capillaries around the bulb a paler plexus in the upper part of the follicle also envelops the sebaceous glands Straight vessels along the middle less vascularized part of the follicle connect the lower with the upper plexus Loops of capillaries form a vascular ring around the orifice of the follicle under the epidermis This collar is continuous with both the vascular loops of the epidermis and the network around the follicle The dermal papilla at the base of each follicle contains a large tuft of capillaries in its center This occupies a much larger part of the papilla than is ordinarily realized These capillaries extend to the walls of the inner side of the follicle and are often practically in contact with the wall

During transition from active state to quiescence the bulb atrophies and the base of the follicle moves upward in the dermis and partially out of the network that surrounds it The dermal papilla also recedes upward and slips away from its central capillary tufts Only part of these capillary nets seems to atrophy most of the vascular material collapses and remains at the base of the resting follicle as a tangled bundle in contact with the free dermal papilla Since only the lower part of the follicle degenerates when it becomes quiescent the palisade of straight vessels in the middle third is unchanged Higher up around the sebaceous gland and the infundibulum the plexus also stays intact When a quiescent follicle becomes active again the new bulb plows its way through the bundle of capillaries and grows inside it

The capillary networks from any part of a follicle and its sebaceous glands form a continuous system and each vascular bed is a unit Since the pilosebaceous system functions as a unit the vascular mechanism may be responsible for this integration or it at least shares the responsibility

The follicles of vellus hairs in the body skin or *in the bald* scalp are surrounded by very simple capillary systems A few capillaries surround the lower part of the follicle but no vessels penetrate the dermal papilla The enormous se

(7) J Nat Cancer Inst 19 451-463 September 1957

baceous glands associated with these follicles are normally highly vascularized

Tonofibrils of Human Epidermis were studied by Arwyn Charles and J. G. Smiddy[8] (Leeds Univ.) by electron mi-



Fig. 5.—Section [illegible] material [illegible] ext[illegible] [illegible] Figure shows part of outline of malpighian cell [illegible] nucleus [illegible] Many prickles [illegible] are seen at [illegible] [illegible] flanked by electron [illegible] Between [illegible] in which tonofibrils *tf* can be distinguished. [illegible] 11,500 [illegible] adjacent cell wall *cw* can sometimes be seen [illegible] (Charles, A., and Smiddy, F. G.: J. Invest. Dermat. [illegible] November 1957.)

croscopy The structure of a typical prickle is shown in Figure 57 Occasionally the electron dense lines are seen to be double and more frequently a dark line is seen to traverse the clear central region The tonofibrils have never been seen to pass through the clear central region

Between the prickles the walls of the adjacent cells are distinct and contiguous and when cut transversely are easily distinguishable as a double line If dehydration is prolonged the walls tend to separate giving rise to intercellular spaces bridged by the prickles which thus form the intercellular bridges seen in light microscopy The walls of adjacent cells are apparently fused at the prickle since cell walls have never been observed to separate at these points and the width of the clear central region of the prickle does not change

At the dermal epidermal junction there is again seen a tonofibrillar tuft but there is no counterbalancing tuft on the other (dermal) side The appearance of the tonofibrillar tuft on the junction wall of the basal layer cells can show some variation in different human material but in essence appears to be half the normal prickle which with its two oppositely situated tufts is the structure invariably seen between epidermal cells

This assumption suggested that both ends of the tonofibril or tonofibrillar bundle are attached to the cell wall the point of attachment being the prickle or half prickle The result of such an arrangement would be to link the whole of the tonofibrillar network of the epidermis into an elastic system eminently suitable for taking up the distortion strains to which the epidermis is constantly subjected The opposite positioning on either side of the area of adhesion of the tonofibrillar tufts of adjacent epidermal cells becomes understandable because this arrangement allows the advantages of the elastic system to be realized the tonofibrillar attachment at the dermal epidermal junction however requires no counterbalancing tuft because the adhesion between dermis and epidermis enables any strain on that point to be transferred to the dermis and to the collagen and elastin fibers found there

(8) J I t Dermat 9 3 7 33 Nov mbe 1957

To study the response of prickles and tonofibrils to stretching, sections were cut parallel and transverse to the direction of stretching of skin fixed in a stretched state. Sections cut parallel to the direction of stretch were found to be cut parallel to the main orientation of the tonofibrils; sections cut transversely to the direction of stretch showed transverse sections of the tonofibril bundles. Tension was found to develop at the points of anchorage of the tonofibrils on the basement membrane with consequent inward puckering of the membrane at these points.

Eleidin in the stratum granulosum accounts for the whiteness of the skin, according to R. Lutembacher[9] (Paris). Mucous membranes, which do not contain eleidin, are transparent, allowing the red color of hemoglobin to be seen. Redness of the lips is also explained by lack of eleidin rather than by special vascularization. The color of the cock's comb is also due to the absence of eleidin, except for the pearly white areas in the region of the auricular orifice and on the wattles, where eleidin granules may be found.

The whiteness of eleidin, which like the tin foil of a mirror reflects light, is comparable to that of boric acid crystal. Dermatologists recognize that in certain pathologic states, as in inflamed scars, the skin may be red owing to transparency due to lack of eleidin. Conversely, mucosal surface may be abnormally white, as in leukoplakia and the white streak of buccal lichen planus, owing to abnormal proliferation of the granular layer and an excess of eleidin. Eleidin also gives psoriasis scales their waxy appearance.

Response of Human Epidermis to Application of Carcinogenic Hydrocarbons was investigated by Murray Guy Williams[1] (Wayne State Univ.). A 1% solution of 3-methylcholanthrene in benzene was applied to the normal epidermis of 11 volunteers. No discernible change was observed clinically after the single application. Microscopically, a slight to moderate increase in mitoses was found during the period of study, viz. the first 7 days after the application.

A 1% solution of 3-methylcholanthrene in benzene was applied to an area of keratin-stripped epidermis. On clinical examination this area did not differ from the results of ordinary cellophane stripping painted with benzene only. The

(9) Presse méd. 65: 175, Dec. 5, 195
(1) J. Invest. Dermat. 30: 13, 0 Ja y 1958

microscopic appearance after keratin stripping and painting with 3 methylcholanthrene was similar to that observed after keratin stripping alone except that the mitotic re pon e in tead of being greater was li,htly lower and prolonged

One volunteer received daily application of 9 10 dimethyl 1,2 benzanthracene in mineral oil for 7 days One and 2 months later a single application produced an allergic papulovesicular response in the test site and in the areas previously painted with 9 10 dimethyl 1,2 benzanthracene This is interpreted as further confirmation that the immunolo,ic ta tu of the host is one factor involved in carcinogenesis

All subjects were followed 2 8 month The keratin tripped and painted areas and biop y ite healed normally

► [This appears to be the first instance in which allergic sensitization to the carcinogen 9 10-d methyl 1,2 benzanthracene has been demonstrated The po sibility has been considered for years that allergic sensitization may play a role in carcinogenesi produced by imple chemical ub tances Experimental investigation in animals thus far ha failed to turn up supporti e evidence (Serri Herrmann and Kirman Acta dermat venereol 34 248 1954) —Ed]

Effect of Oxypsoralen on Ultraviolet Carcinogenesis in Albino Mice wa studied by M A O Neal and A C Griffin (Univ of Texas) Swiss mice were totally irradiated with ultraviolet lamps for 15 minutes/day The final incidence of ear tumors in mice receiving 8 methoxyp oralen (8 MP) in their diet wa considerably les than that of control The extent of protection afforded by the compound ap peared to be proportional to its concentration in the diet up to an optimal level of 0 5 Gm 8 MP/kg diet Ear tumors oc curred in 32% of mice receiving this concentration in 39% of those receiving 1 Gm 8 MP/kg diet and in 45% of tho e receiving 0 2 Gm /kg

The final tumor incidence in mice receiving intraperitoneal injections of 0 4 mg 8 MP daily 1 hour before ultraviolet exposure was nearly 100 % compared with 68 % in the control group An accelerated latent period of carcinogene is was al o ob erved When the compound was administered in the same do age 20 hours before irradiation the final ear tumor incidence was in the same range as that of the control

There i no complete explanation for the results of the e tudies The concentration of 8-MP i a definite factor a i

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(9) Presse med 65 375 Dec 5 1957
(1) J Invest Dermat 30 13 0 January 1958

► [The results with 8 MP feedings suggest a protective effect whereas those with intraperitoneal injections indicate an increased incidence of cancer formation in mice with ultraviolet light irradiation In any event they support the viewpoint that it is not justified at this time to recommend 8-MP tablets in man for their protective effects against the burning rays of natural sunlight —Ed]

Hitherto Unreported Malignant Melanomas in Syrian Hamster Experimental Counterpart of Human Malignant Melanomas Joseph G Fortner and Arthur C Allen[3] (Sloan Kettering Inst) found primary melanotic and amelanotic melanomas in 10 (1 9%) of 523 Syrian hamsters surviving 181 days or longer Three melanomas occurred in untreated control 2 in animals inoculated with bile from patients with cancer of the extrahepatic biliary tree 2 in animals given injections of sodium desoxycholate solution and 1 each in those given injections of ox bile bile from patients with non malignant biliary tract disease and sesame oil The tumors are considered to be of spontaneous origin since they occurred in untreated controls and in animal subjected to various experimental conditions Of the 10 tumors 8 occurred in male Two were grossly melanotic and 8 amelanotic A separate second primary tumor was found in 5 of the 10 hamster with malignant melanoma Metastase were found in 9 hamster

Though malignant melanomas have been described in many other animal species this is the first experiment recorded in which they were observed in the Syrian hamster The histogenesis of the hamster melanocarcinomas appears to be identical with that of malignant melanoma in man i e origin from a junctional nevus Except for one feature the histologic appearance of the hamster melanoma corresponds well with that of human tumors In both there is a wide range of pleomorphism mitotic figures and pigment content In both the metastases may be overwhelmingly wide spread However there is a disparity in the relation between pigment content and degree of anaplasia and growth potential In malignant melanomas of man there appears to be no relation between melanin content of the primary tumor and degree of anaplasia of tumor cell or their capacity to metastasize Contrarily the pigmented melanomas of hamster apparently as in mice are far more innocuous appearing histologically than the amelanotic tumors The

(3) Cancer Res 18 98 104 January 1958

time of administration with reference to the ultraviolet exposure. Early erythema response to ultraviolet may be important in tumor formation. Animals receiving 8 MP 1 hour before irradiation exhibited severe erythema of the ear, face and tail with subsequent scar formation and shriveling of the ears. These preliminary changes were less marked in the control groups, whereas the ears of mice receiving dietary psoralen maintained a relatively normal appearance throughout the entire period of irradiation (110 days). The early damage to the ears may produce irreversible changes which, with the continued stimulation of ultraviolet light, lead to neoplastic transformation.

Since little is known concerning the metabolism of 8 MP, it is difficult to explain adequately its mechanism of action. The protective effect afforded by oral administration of the compound might be explained by the strong absorption of this compound in ultraviolet wavelengths (3,000 and 2,500 A). The concentration of this or related compounds in the outer layers of the skin may effectively filter out the ultraviolet rays. Recently the authors observed that the shorter ultraviolet rays (2,537 A) have no effect on the action of 8 MP in the formation of pigmentation or other erythema changes. In contrast, severe erythema changes were found in man and animals after oral administration of 8 MP and subsequent exposure to longer ultraviolet rays. The possibility exists, however, that with oral administration the compounds are metabolized in the intestinal tract or liver. The resulting metabolites might exert a protective effect in the skin, possibly by forming complexes which would act as a barrier to incident ultraviolet light.

Since 8 MP absorbs strongly in the ultraviolet wavelengths, the enhancing effect produced by intraperitoneal injection might be due to an immediate concentration of this compound in the skin, resulting in an increased photosensitivity to ultraviolet light. It is unlikely that a metabolite is responsible for this action, since 8 MP given in the same dose 20 hours before ultraviolet exposure is without effect, indicating that it has been metabolized to inactive products or possibly excreted unchanged. These findings parallel the results of human studies. 8 MP does not promote pigmentation in man if there is a lapse of 20 hours between administration and exposure to sun.

fore sweating was replaced by concentration in the apical part of the secretory cell and around the vacuole Nuclei of the small dark cell increased in size and showed a more prominent nuclear membrane Nuclei of the large pale cells virtually lost their membrane and contained less chromatin and were le ba ophilic than those in control specimen After several hours of sweating the basement membrane of the secretory coil thickened After 1 hour of sweating there was decrease of glycogen in the secretory cell and after 3 6 hours glycogen di appeared from most of the cells After 6 hours there was definite increase in the activity of esterase

The cytologic alterations ob erved as the result of profuse sweating were greater than anticipated It seems unlikely that such a normal function as secretion of sweat could produce frank damage to the secretory cells of the gland I o sibly the eccrine sweat gland has limited ability to maintain profuse secretion This is reflected in the fairly rapid change in sodium potassium and chloride concentration of sweat and its rate of output noted as a result of acute expo ure to a hot humid environment

Human sweat glands have been divided into two types tho e with imple fluid ecretion the eccrine sweat gland and tho e in which part of the cell is secreted the apocrine glands This tudy hows that eccrine glands al o have a particulate secretion (PAS positive nonglycogen material) Definition of the term eccrine and apocrine on the basis of a fundamental difference in the method of excretion may be erroneou However a change in nomenclature is not advocated because the e terms if not taken literally retain u efulnes in differentiating these embryologically and anatomically different type of sweat glands

II Recovery from effects of profuse sweating was investigated by Dob on and Lobitz who studied punch biopsy pecimen from normal young men before and after 6 hours of profu e sweating in a heat cabinet At 24 hours after sweating the cells of the secretory coil appeared larger than immediately after sweating although atrophy and general di tortion of the secretory coil was apparent Glycogen was present in the large pale cell but had not reappeared in the cells of the duct There was slight increase in the amount of PAS po itive diasta e re istant granules within the secre

(3) J I t Dermat 1 07 213 Oct be 1958

capacity of amelanotic tumors in hamsters to grow and metastasize far exceeds that of the pigmented tumors

With rare exceptions tumor implants of hamster melanoma have grown in all animals inoculated The nearly uniform takes of implants rapid but individual growth rates of melanotic and amelanotic types and similarity to the human melanocarcinomas all result in a biologic spectrum of the melanocarcinoma which should provide a useful baseline for further investigation

Some Histochemical Observations on Human Eccrine Sweat Glands—*III Effect of profuse sweating* was studied by Richard L Dobson Victor Formisano Walter C Lobitz Jr and Doris Brophy[4] (Dartmouth Med School)

METHOD—Maximal sweating was gradually induced in normal young men in a heat cabinet in which the temperature rose from 70 to about 105 F Maximum temperature was maintained 6 hours or until total failure of the sweat glands or pronounced subjective symptoms required stopping of the experiment Biopsy specimens were obtained without anesthesia by high speed rotary punch before at hourly intervals during and immediately after 6 hours of profuse sweating

Maximal generalized sweating was elicited within 30 minutes Sweating was profuse for about 4 hours then declined At this time the subjects became restless and uncomfortable despite adequate fluid and electrolyte intake Between the 5th and 6th hours as sweating became scanty or ceased the subjects showed lassitude and malaise This was accompanied by tachycardia hyperpnea and orthostatic hypotension

Marked alterations in the structure of the eccrine sweat glands occurred After 1 hour there was a striking depletion of PAS positive nonglycogen particles in the cells of the secretory coil After 4 6 hours only the luminal border of a few secretory cells contained significant numbers of these particles The particles were excreted directly into the lumen of the secretory coil and gradually traversed the duct until they reached the surface After about 1½ hours of sweating vacuoles appeared along the basal border of the glandular cells and in the cells of the coil portion of the duct adjacent to the nuclei The secretory cells especially the large pale cell definitely decreased in size Prominent intracytoplasmic inclusions were noted in the secretory cells after 6 hours of sweating The even distribution of mitochondria noted be

(4) J Invest Derm 31 14 159 September 1958

excised after progressive time intervals No sensitization appeared when the nodes were excised within 48 hours after the primary contact When they were excised after 3 5 7 and 8 days sensitization was observed in 20 50 80 and 90% of the animals respectively To sensitize the animal the explant must be kept in situ for at least 2 days The time of contact required to sensitize guinea pigs varied between 12 and 48 hours for the explant On the normal skin it takes about 8 32 hours

To examine the influence of the regional lymph nodes on the maintenance of sensitization the authors also sensitized animals by applying dinitrochlorobenzene to a cutaneous explant then excised the regional lymph nodes 21 12 11 9 and 8 days after the primary contact and tested the animal 1 month later Sensitization was not eliminated by this intervention i e no animal was desensitized

The fact that sensitization does not appear when the regional lymph nodes are excised 48 hours after the primary contact suggests the production of antibodies in the nodes Even when the nodes were excised after 7 days sensitization did not develop in 17% of the animals The fact that sensitization is maintained when the regional lymph nodes are excised 8 21 days after the primary contact implies that antibodies are produced in other organs Sensitization was maintained in 41 / of the sensitized animals the nodes of which had only been functioning for 6 days The authors believe that antibodies are produced in regional lymph nodes as well as in other organs and do not believe that the role of the lymph nodes is only to lead the antigen to the organism

Influence of Certain Neurotropic Drugs on Dinitrochloro benzene Eczema in the Guinea Pig was studied by P de Graciansky I Israel and J Cohen Solal[7] (Paris)

METHOD —Sensitization of guinea pigs was achieved by daily application for 12 18 days of 0 05 cc of 0 135% solution of dinitrochlorobenzene (DNCB) After sensitization had been shown its intensity was estimated by the quantitative technic of Frey On areas on the flank epilated with scissors 0 05 cc of solutions of 0 01 0 03 0 05 0 1 0 13 0 15 0 175 and 0 2% DNCB were applied When positive reaction was obtained on one of the surfaces it was allowed to disappear (? days) before the same quantity of the next lower concentration was applied on another site The threshold of sensitivity corresponded to the lowest concentration capable of provoking a definite response in 4-48 hours Because the initial threshold did not nec

(7) B J Dermat 70 345 353 October 1958

tory cells Metachromasia was either minimal or absent

At 48 hours despite great variability in cellular configuration within the secretory coil, reaccumulation of glycogen and PAS positive diastase resistant material was relatively constant Within the duct, glycogen reappeared only in the basal cells in most instances whereas within the secretory cell glycogen content was normal The amount of PAS positive diastase resistant material within the small dark cells was greater than at 24 hours but still less than in control specimens Metachromasia was minimal or absent

At 72 hours glycogen had appeared in the luminal cell of the duct Secretory cells were less atrophic and most of the secretory coils appeared normal in configuration Increase in the amount of PAS positive diastase resistant material had continued and many cells showed concentration of this material along the luminal border of the cell After 5 7 days all the secretory coils and ducts examined appeared normal

Probably the most important and potentially useful aspect of this study is the observation of a difference in the recovery rate of the large pale cells and the small dark cells in *the secretory coil* and *a difference in the time of reappearance* of glycogen in the secretory coil and the duct Taking advantage of these convenient circumstances may make it possible to characterize the processes of secretion and absorption within the eccrine sweat gland

► [What happens to the sweat glands and to the systemic alteration that are a consequence of the changes in the sweat glands (produced by profuse sweating) when the experimental subjects remain in the hot environment? To what extent do they adjust How long does it take to make the adjustment? Does adjustment continue indefinitely? The question may soon be answered if studies such a the e are continued ——Ed]

Role of Regional Lymph Nodes in Development of Dinitrochlorobenzene Contact Eczema in Guinea Pig was studied by J R Frey and P Wenk[6] (Basel) For the primary contact with dinitrochlorobenzene an isolated skin piece or explant was used The explants were connected with the animal body either by a pedicle containing arteries veins and nerves or by an additional skin bridge Thus the function of the vascular nervous and lymphatic systems in the development of contact eczema could be studied individually

The animals were sensitized by applying the dinitrochlorobenzene to the explant The regional lymph nodes were

(6) Dermatologica 116 243 59 Apr May 1958

skin sensitization to a poison ivy allergen pentadecylcatechol (PDC) and of experimentally induced skin sensitization to 2 chemical sensitizers 2 4 dinitrochlorobenzene (DNCB) and paranitrosodimethyl aniline (NDMA) in 23 patients with sarcoidosis and 135 control subjects

With PDC the most potent sensitizer there was no significant difference in the incidence of sensitization in patients with sarcoidosis and in control With DNCB and NDMA a highly significant decrease in frequency of sensitization was observed in patients with sarcoidosis compared to the controls Dinitrochlorobenzene was about half as effective in sensitizing patients with sarcoidosis as in controls whereas NDMA the least potent allergen used was about one fourth as effective

These findings demonstrate that the lowered incidence of reactivity characteristic of sarcoidosis is not apparent when a strong sensitizer such as PDC is used It is only with weaker allergens that the difference becomes apparent Actually DNCB and NDMA are considerably more potent than commonly encountered contact allergens such as formalin Vioform® and heavy metals Thus a much lower incidence of contact sensitization might be expected in patients with sarcoidosis if these latter compounds were to be tested

Patients with sarcoidosis are capable of reacting to these and other skin test antigens although the incidence of sensitization is decreased For this reason the use of batteries of such tests probably has little diagnostic value in sarcoidosis

▶ [This work proves that in sarcoidosis there is a diminished capacity to become sensitized or react not only to tuberculin type allergens but also to eczematogenic contact allergens —Eds]

Experimental Eczema Eczematous Reaction Elicited during Sensitization of Guinea Pig M Golay and I Brun[9] (Univ of Geneva) administered to the necks of male guinea pigs weighing about 300 Gm 1 18 daily applications of 1% dinitrochlorobenzene in acetone and then tested the nipples by application of an 0 1% solution of the same compound at the time of last application to the neck The nipples were excised 24 hours later for histologic study

With the 3d application or 2 days after beginning sensitizing treatment slight spongiosis was already evident After 5 days eczematous lesions of the epidermis were observed regularly and were as pronounced as when the tests

(9) Derm t logic 116 408-412 J 1958

essarily prove stable the test was continued for several weeks usually.4 6

Of 88 animals sensitized satisfactorily 25 served as controls and spontaneous variations of threshold were followed in each Daily subcutaneous injections of 2 5 mg d amphetamine and 5 mg caffeine were given to 37 animals and daily injections of 30 mg chloral hydrate to 26 In each group variations in threshold were followed

Among the controls 13 (52%) of the guinea pigs showed a stable threshold 11 (44%) a slowly rising threshold and 1 (4%) a falling threshold Of the animals treated with caffeine and d amphetamine a stable threshold was observed in 9 (24%) a falling threshold in 26 (71%) and a rising threshold in 2 (5%) Of the animals treated with chloral hydrate a stable threshold was noted in 2 (7%) a rising threshold in 21 (82%) and a falling threshold in 3 (11%) Thus there was heightening of sensitivity by stimulating drugs and lowering of sensitivity by sedatives The drugs used were chosen for their action on the central nervous system particularly at the cortical level and for their lack of peripheral action The effects observed on the threshold of sensitivity could not be attributed to peripheral vascular changes Instead the modification of sensitivity apparently resulted from central nervous system activity effects which could be predicted from clinical observations and the general laws of cortical function

These experiments underline the individual character in the development of sensitization its degree and course in the laboratory animal This feature brings the conditions of experiment close to those of contact eczema observed in man The influence of centrally acting drugs on the development of the allergic state shows that the central nervous system modifies the response to the allergen and that it represents an important component of what it is customary to call the soil These conclusions are valid no matter what may be the mechanism determining the eczema and whether or not it is accepted as an antigen antibody reaction

► [With the doses of sedatives or stimulants customarily used in clinical practice in man we have not been impressed by any alterations in the severity of allergic contact dermatitis The doses of drug given the guinea pigs in these experiments would correspond to the following daily approximate doses in a 150 lb person 375 mg d amphetamine 0 7 Gm caffeine and 4 5 Gm chloral hydrate!—Eds]

Induction of Allergic Contact Dermatitis in Patients with Sarcoidosis William L Epstein and Robert L Mayock* (Univ of Pennsylvania) determined the incidence of natural

(8) Proc Soc Exper Biol & Med 96 96 8 December 1957

phene exceeded those to sodium zirconium lactate alone Acute inflammatory reactions and typical granulomatous lesions also occurred after sub or intracutaneous injection of sodium stearate With both sodium zirconium lactate and sodium stearate inflammatory reactions appeared particularly severe around hair follicles Injection of hexachlorophene alone or a hexachlorophene diethylene glycol mixture produced moderate inflammatory reactions without necrosis and ulceration

Percutaneous application of sodium zirconium lactate 9.2% and hexachlorophene 0.5% in aqueous solution produced acute inflammatory reactions with a tendency to formation of pink papules and nodules The severity of inflammatory reaction following percutaneous applications was markedly enhanced by defatting the skin trauma or repeated applications of the test chemicals

► [These studies fail to answer the important basic question why do a small percentage of those who use zirconium-containing deodorant sticks develop allergic zirconium granulomas whereas apparently not one person who has used a zirconium containing cream or lotion for allergic contact dermatitis due to poison ivy has been reported to have developed such a granuloma Is it the different terrain? The different vehicles and other ingredients in these preparations? Preceding trauma by shaving in the axilla? Friction and massaging which are unavoidable in the axilla? Or one of the many other possible differences between deodorant stick and ointment or lotion and between axillae and skin areas usually affected by poison ivy dermatitis? Or perhaps to chemical differences in the sodium zirconium lactate which is known to possess numerous contaminants in trace amounts? —Ed]

Induction of Allergic Contact Dermatitis in Patients with Lymphoma Leukemia Complex was attempted experimentally by William L. Epstein (Univ of Pennsylvania) Two potent sensitizer 2 4 dinitrochlorobenzene (DNCB) and paranitrosodimethyl aniline (NDMA) were applied to the skin of 27 patients with the following diseases Hodgkin s disease lymphosarcoma myelogenous leukemia lymphocytic leukemia multiple myeloma and extensive mycosis fungoide To determine whether sensitization had occurred the patient were retested 30 days later by a similar application at new sites with a 1 1000 dilution of each sensitizer in acetone Because previous studies have indicated that a racial difference exists in the response to contact allergens the

( ) J I est Derm t 30 39-40 J y 1958

were made after additional sensitization applications No lymphocytic infiltration was found even when the nipple reaction was produced 8 17 days after beginning of sensitization but there was a marked increase of histiocytes Except in 1 case in which it appeared earlier this histiocytic proliferation did not appear until 5 days after sensitization began

These experiments show that the incubation period for an eczema produced at a site of challenge distant from the site of contact sensitization is short i e, 2 3 days Frey and Wenk reported a period of 6 9 days based on macroscopic findings instead of histologic changes

► [It would be interesting to note whether or not the same very early histologic tissue response would occur at skin sites other than the specialized tissues of the guinea pigs nipples The absence of mononuclear cells in the cutis and epidermis is noteworthy Perhaps this is also due to the special site tested Macroscopically evidence of contact type sensitization usually cannot be demonstrated until after a minimum of 5 days incubation period —Eds]

Pathologic Changes Associated with Deodorant Preparations Containing Sodium Zirconium Lactate Experimental Study is presented by John T Prior Herman Rustad and G A Cronk[1] (State Univ of New York Syracuse) Several zirconium compounds have been used in experimental diagnostic and therapeutic medicine for several years One of the most important is hydrous zirconium oxide which has been used in large quantities in treating poison ivy dermatitis To date there has been no evidence of toxicity following use of this preparation Recently sodium zirconium lactate has been combined with other agents such as sodium stearate hexachlorophene alcohol glycerine water perfume and varying amounts of other ingredients and marketed as a deodorant Reports have appeared of granulomatous inflammatory reactions following use of this type of deodorant for a few days to several months Sodium zirconium lactate is used in the commercial preparations in 20 25% strength

The authors found that when injected sub and intracutaneously in rabbits 42% sodium zirconium lactate solution caused marked inflammatory reaction with necrosis of the skin and eschar formation Reactions following injection of solutions containing 12 6 10 5 8 4 6 3 and 4 2% were similar to those observed with 42% but less severe Tissue reactions to a mixture of sodium zirconium lactate and hexachloro

(1) J In e t Dermat 9 449 463 Dec mber 195

phene exceeded those to sodium zirconium lactate alone Acute inflammatory reactions and typical granulomatous lesions al o occurred after sub or intracutaneous injection of odium stearate With both sodium zirconium lactate and sodium stearate inflammatory reactions appeared particu larly severe around hair follicles Injection of hexachloro phene alone or a hexachlorophene diethylene glycol mixture produced moderate inflammatory reactions without necro sis and ulceration

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( ) J I t Derm t 30 39 40 J y 1958

Negro (10 patients) and white (17 patients) groups were evaluated separately.

Sensitization to both DNCB and NDMA was markedly reduced in patients with the lymphoma leukemia complex. Reactions were observed in 31% of the white patients with DNCB and 6% with NDMA. In the white controls 83% reacted to DNCB and 70% to NDMA. In the Negroes with lymphoma leukemia complex 10% reacted to DNCB and 30% to NDMA. Reactions occurred in 61% of Negro controls with DNCB and 45% with NDMA. In all only 2 white patients (12%) reacted to both allergens, whereas the expected frequency among healthy persons is 64% for whites and about 35% for Negroes. Also the intensity of sensitization as indicated by the degree of inflammation was depressed in patients with lymphoma leukemia complex. Not 1 patient had a patch test reaction greater than 2+ and most showed weak borderline reactions.

The diminished susceptibility to contact sensitization corresponds with the lowered reactivity shown by these patients to other delayed type antigens. The significance of this diminished capacity for delayed reactivity is not understood. The most popular explanation is that the cells responsible for producing delayed "antibodies" are crowded out by neoplastic nonantibody forming reticulum cells. However this concept must remain a speculation as long as the site of synthesis of delayed "antibodies" is unknown.

Effect of Feeding Simple Chemical Allergens to Pregnant Guinea Pigs on *Sensitizability of Their Offspring* was studied by Rudolf L. Baer, Stanley A. Rosenthal and Blanka Hagel[3] (New York Univ. Post Grad. Med. School and Skin and Cancer Unit). Groups of pregnant albino guinea pigs were force fed olive oil solutions of picryl chloride (PC) or dinitrochlorobenzene (DNCB). Pregnant control animals were fed olive oil alone. Several weeks after birth the offspring were sensitized to the allergen fed the mothers. After a 4 week incubation period all guinea pigs were simultaneously tested with dilutions of the allergen to which they were sensitized. Offspring born to animals fed solutions of PC or DNCB during gestation had a slightly though consistently lower capacity to become sensitized to the homologous allergen than did the offspring of mothers not fed the

(3) J. Immunol. 80 4 9-434, June 1958

allergen In 17 of 18 test sites with different dilutions the averages of the reactions of the offspring of allergen fed mothers were weaker than those of the control animals off pring

The authors infer that the feedings of the allergen to the pregnant guinea pigs may have had a slight effect on the sensitizability of the offspring This is supported by results of deliberate sensitization to citraconic anhydride a chemically unrelated sub tance in the same animals With this compound there was no uniform trend toward lesser sensitizability in either the test animals born of mothers exposed to one of the two other allergens or the control animals Further the differences between test and control animals in the averages of the reactions to citraconic anhydride were less than those noted between the test and control animals sen itized to PC and DNCB This also suggests that the differences ob erved in the sensitizability of animals born to allergen fed mother and control animals are ba ed on a specific effect rather than on chance The re ults of these experiments are not conclu ive but they are sufficiently suggestive of some specific le sening of sensitizability to encourage further tudies in this important field of investigation

[These results are suggestive of slight inhibit on of sensitizability and are not conclu i e evidence that specific acquired tolerance was produced Howe er recently it has been found also that guinea pig fetuses injected with tubercul n have a d minished susceptibility to become sensitized to tuberculin in adult life as compared with control animals

The findings of the authors with simple chemical contact allergens and of Weiss (J Exper Med 10 83 1958) with tuberculin lend further evidence to the marker theory of Burnet He attempted to explain why animals do not form antibodies against their own antigenic tissues even though they do so against the tis ues of other an mals According to this theory an mal in fetal life learn to recognize and mark their body own mate ri is a peculiarly their own and therefore they fail to form antibodies agai st them in postfetal life He theorized that this mechanism might apply even to entirely foreign materials as long as exposure to them took place a ci lentally or deliberately during fetal life —Ed]

Experimental Toxic and Allergic Contact Dermatitis — 1 *Chemical study of histamine content* —Using an adaptation f the microchemical method of Lowry and co workers J Frochazka Fi her and Robert A Cooke[4] (Roosevelt Ho p New York) with the technical assistance of Sonya Strosman and Gloria Cordon found the histamine content of normal guinea pig kin to be 2-6 µg (average 4 3 µg) At the sites of allergic dermatitis in sensitized guinea pigs

(4) J All rg 29 396-413 Septembe 1958

after epicutaneous application of 0 1% dinitrochlorobenzene (DNCB), a steady rise in histamine was observed beginning after the challenge and reaching a maximum at 48 hours At this time the histamine content averaged over 400% above normal Insignificant changes were observed in the histamine content of lesions of toxic dermatitis induced in normal guinea pigs by application of 2% DNCB, but in those induced by 5% DNCB the histamine content increased to a maximum about 80% above normal 48 72 hours after application Thus the increase in histamine content was much less than that observed in allergic dermatitis

The infiltrating cells observed in guinea pigs with experimental allergic dermatitis were mononuclear cell, whereas in toxic dermatitis they were both polymorphonuclear and mononuclear cells in about the same proportion as found in blood There was no significant difference in the number of cells found at the sites of allergic dermatitis due to 0 1% DNCB and toxic dermatitis due to 5% DNCB Leukocytes in normal and sensitized animals contained the same amount of pre formed histamine and no significant changes in the histamine content of whole blood were observed during or after an allergic reaction The qualitative cellular difference in the infiltrate at the sites of toxic versus allergic dermatitis seems too small to explain the marked difference in histamine levels in the two different inflammatory reactions Thus it may be assumed that the infiltrating mononuclear cells of sensitized animals have the capacity on minute specific stimulation with an antigen to activate histamine metabolism at the site of an allergic inflammation by promoting histamine synthesis inhibiting histamine breakdown, or both

Much less histamine was found in allergic lesions of guinea pigs given injections of germanin Apparently germanin an inhibitor of histamine formation from l histidine interferes with decarboxylation at the site of allergic dermatitis This supports the assumption that the histamine accumulation in allergic dermatitis is induced by activation of histamine metabolism Allergic lesions in guinea pig given injections of germanin lasted much longer than allergic lesions in animals not given this drug This suggests that histamine is an accelerator in the repair process rather than a causal factor in these allergic reaction

II Histopathologic study.—Fisher and Cooke[5] with the technical assistance of Stroyman and Gordon induced toxic dermatitis in normal guinea pigs by application of 5% DNCB Allergic dermatitis resulted from application of 0 01 or 0 1% DNCB to the skin of guinea pigs sensitized to this chemical The 3 12 hour lesions of toxic dermatitis showed epidermal injury always accompanied by scant extravasation of polymorphonuclear and mononuclear cells The 3 12 hour lesions of allergic dermatitis showed massive extravasation of mononuclear cells migrating in trails directly into the epidermis Thus the concentrated chemical caused relatively sparse infiltration in the toxic reaction whereas dilute DNCB induced massive infiltration with direct ascent of the mononuclear cells toward the challenged skin surface The most plausible explanation for the behavior of the mononuclear cells seems to be that the sensitization induced in them a capacity for positive chemotaxis i e a faculty for detection of a chemical (or its protein derivative) in minute concentrations and for migration straight into the area of highest concentration

Most toxic lesions at 24-48 hours showed an increase of polymorphonuclear and mononuclear cells in the dermis after the earlier death of epidermal cells Allergic lesions at 24-48 hours showed massive invasion of the epidermis by mononuclear cells and formation of vacuoles In some lesions microvesicles formed presumably at points of fusion of vacuoles Vacuolation and vesiculation cause disruption of the epidermis apparently leading to its death and exfoliation Mononuclear cell invasion vacuolation vesicle formation and exfoliation of the epidermis are steps in a process characteristic of the allergic response not seen in toxic lesions Histamine accumulation and increased phosphatase activity also occur in allergic but not in toxic lesions Thus allergic reactions show not only a specific cellular response but also a characteristic intensity in local metabolic activity enzymatic in character

The results suggest that the allergic reaction depends on mononuclear leukocytes which acquire specific capacities through sensitization However histologic findings at sites of allergic dermatitis on guinea pigs given injections of germanin indicate sensitization also of epidermal cells In all

(5) J Allergy 9 411 4 September 1958

animals treated with germanin the 48 hour allergic lesion revealed considerable dermal infiltration by mononuclear cells However the epidermis was extremely thickened and not invaded by these cells It seems that germanin prevents ascent of the mononuclear cells in the epidermis The extreme epidermal thickening might be regarded as the allergic response of epidermal cells after participation of the mononuclear cells has been forestalled

► [*These findings confirm the observations in guinea pigs of our group* (J Invest Dermat 27 249 1956 and A M A Arch Dermat 76 549 1957) Jadassohn's group (Acta dermat venereol 36 360 1956 and Dermatologica 114 91 1957) and Nilzen's group (Acta dermat venereol 35 292 1955)

The new finding is the striking increase in histamine content of allergically reacting skin and much less striking increase in skin reacting on a *primary irritant* basis The explanation that the monocytes of sensitized animals have the capacity to activate histamine metabolism at the site of an allergic inflammation is not likely to be correct as our own studies have shown that the type of damage occurring in primary irritant reactions is in principle different from that seen in the allergic response One is a primarily parenchymatous reaction and the other is one of intercellular edema Since the intercellular edema appears even before masses of mononuclear cells have arrived in the intercellular spaces in the epidermis the mononuclear migration probably is a consequence rather than a cause of the changes This makes it unlikely that the mononuclear cells are the immediate cause of the increase in histamine content

The very significant effect of germanin on the allergic response to DNCB also is a new finding The mechanism which produced the acanthosis in the animals given injections of germanin at the DNCB sites needs further elucidation before one can accept the interpretation that the acanthosis is an altered form of allergic epidermal response —Ed]

Influence of Selenium Disulfide on Sebaceous Gland Volume in Guinea Pigs was investigated by Erik Skog[6] (Univ of Cincinnati) Guinea pig skin was exposed to selenium disulfide shampoo (Selsun®) and to the shampoo *vehicle only* Shampoo treatment was repeated 10 times at intervals of 2 3 days Biopsy specimens were excised before and after the course of treatment and the volume of the sebaceous gland was determined as described by Rothman and associates

Selenium disulfide *shampoo and the shampoo vehicle alone* caused considerable increase in the volume of sebaceous glands but the effect of the selenium shampoo was more pronounced Treated epidermis was thicker than untreated epidermis The latter had 3 or 4 cell layers whereas treated epidermis had 5 9 layers Most of the cell proliferation was confined to the prickle cell layer Such acanthogenic action is also exerted by various kind of detergents The shampoo

(6) Acta dermat venereol 38 15 19 1958

contains a high percentage of Nacconol* an alkyl benzene sulfonate detergent having marked acanthogenic activity The effect was not confined solely to the superficial layers of the epidermis but occurred also in the follicles which became much wider than normal Synthetic detergents may exert the same hyperplastic action on the sebaceous glands as they do on the epidermis The results of the investigation suggest that the effect is potentiated by selenium disulfide

► [This investigation provides a possible explanation for the excessive oiliness of the scalp and scalp hair which occurs in about 30% of persons who shampoo with Selsun* Suspension Recently Sulzberger called attention to the apparent increase in the incidence of a somewhat patterned diffuse alopecia of the scalp in young and middle aged women During recent years this type of hair loss has been noted with increasing frequency by many dermatologists in the United States and Europe Of course many possible etiologic factors have been considered e g the prolonged and repeated exposure to the acanthogenic action of certain detergents in Selsun and many other shampoos which have been sold during the past 10 years or so But neither this nor the nylon brushes reported on by Savill (see p 267) are likely to be the causative agents of this particular type of thinning of the scalp hair —Eds]

Effect of Temperature on Production of Herpes Simplex Virus in Tissue Culture was investigated by Clayton E Wheeler (Univ of Virginia) Cultures of HeLa and AU cells infected with 3 strains of herpes simplex virus and incubated at 4 different temperatures for 3 days were observed for cytopathogenic effects and titrated for virus content Little or no virus production was found in cultures incubated at room temperature (20 5 27 7 C) Greater amounts of virus were produced at 30 and 40 C and the greatest amount was produced at 35 C Cultures of HeLa cells which were incubated at room temperature and showed little or no evidence of virus production (few or no herpes plaques and little or no titratable virus) promptly produced increased amount of virus when the incubation temperature was raised to 35 C Incubation of herpes virus in blanks (culture tube containing medium but no cells) at 40 C resulted in complete loss of virus Small amounts of virus survived incubation at 35 C more survived at 30 C and the greatest amount survived at room temperature

Present data show that incubation temperature has a profound effect on the amount of herpes virus present in pooled cells and medium at the end of 3 days incubation Studies of virus host systems other than those involving herpes sim

(J Immun 81 98 106 July 1958)

plex indicate that temperature has an important effect on the amount of virus produced In a number of animal virus host systems, the optimum temperature range is 35 37 C (influenza yellow fever vesicular stomatitis myxoma vaccinia variola and ectromelia) and higher incubation temperatures result in less virus production or its cessation It is not clear in most instances whether the lower yield of virus at higher temperatures is due to greater virus inactivation or to less virus production or a combination of both All animal virus host systems do not respond identically to variations of temperature and plant virus host systems show considerable variation in optimum temperature of incubation

Results of the present study might apply to the problem of recurrent herpes simplex infections in man following elevation of body temperature Elevation of body temperature increases the temperature of skin cells If a few of these skin cells contain herpes simplex virus in some form (latent or inapparent infections) a temperature rise might result in temporary increased production of herpes virus which becomes manifest as the clinical disease The mechanism of recurrent herpes simplex infections probably is not this simple but the possibility provides an entering wedge for further study

► [The great variety of factors known to precipitate recurrences of herpes simplex lesions makes it likely that several mechanisms produce these recurrences Wheeler s work suggests at least one possible mechanism since the local increases in temperature resulting from trauma sun exposure inflammatory processes allergic reactions etc may be one of these trigger factors for recurrent herpes simplex —Ed]

Long term Tissue Culture of Epithelial Like Cells from Human Skin Clayton E Wheeler Charles M Canby and Edward P Cawley[8] (Univ of Virginia) after incubation of trypsinized material from human skin for 31 days found a small colony of epithelial like cells in one of the tubes The cells continued to multiply A few were removed 45 days after planting and transferred to other tubes where they continued to multiply rapidly and maintain an epithelial like appearance The cells have been grown continuously for 9 months and 30 subcultures have been made An enormous number of cells has been grown from the original colony The medium used for growth was 40% pooled human serum 5% chick embryo extract and 55% balanced salt solution con

(8) J Invest Dermat. 9 383 39 November 1957

taining 100 units of penicillin and 100 µg streptomycin/cc

The line of cells (referred to as AU cells) when grown on cover slips and stained with hematoxylin and eosin resembled so closely those of epidermoid carcinomas of anaplastic type as to be indistinguishable The AU cells showed variations in size shape and staining qualities Mitotic figures and abnormal mitoses were frequent

The AU cells resemble HeLa cells in their rapid growth and ease with which they can be transplanted Microscopically most AU cell cultures are indistinguishable from those of HeLa cells in the unstained and stained states The AU cells however are not quite as stable or fast growing as HeLa cells

The new AU cell line supports the growth and multiplication of three strains of herpes simplex virus Vaccinia virus has also been shown to proliferate in AU cells but the authors have been unable to demonstrate cytopathogenic change in AU cells after addition of the virus of ecthyma contagiosum or of tissue from a milkers nodule

The isolation of cells having the morphologic characteristics of malignant cells in tissue culture from normal human tissue has been reported by a number of authors Cells with growth and morphologic characteristics similar to those of AU cells have been isolated from normal skin conjunctiva foreskin appendix intestines kidney liver bone marrow and nasal mucosa Although the cells of these lines grow rapidly show increased capacity for anaerobic glycolysis and have morphologic characteristics of malignant cells they have not been proved to be actually malignant

The exact site or cell of origin of the various cell lines is unknown Their morphology suggests an epithelial origin but their tissue sources do not exclude origin from connective tissue blood vessels nerve sheaths or other structures Whether these cells represent mutations from normal cells whether something in the growth medium exerts a carcinogenic effect or whether there are inhibitor substances in the intact animal not present in vitro that prevent malignant change are unexplored possibilities

► [The results observed by Wheeler Canty and Cawley pose many questions Of course there is a big difference between tissue culture skin cells and cells in the living human skin Nevertheless one must suspect that perhaps epidermal cells are more pluripotential than orthodox teaching would permit one to believe and that it is possible some or many or all cells

of the skin (and other organs?) have the potential for malignant changes and that it is certain growth controlling (inhibitory) factors present in living skin which prevent malignant changes from supervening The latter possibility no longer seems so farfetched in view of the finding of the Sloan Kettering Institute group that patients with malignant tumors have a distinctly decreased resistance to growth and invasion by cultured malignant cells as compared with subjects without malignant tumors —Eds]

Evidence for Humoral Mechanism Which Prevents Growth of Dermatophytes in living tissues below the water electrolyte barrier of the skin is presented by Allan L Lorincz Joseph O Priestley (Univ of Chicago) and Paul H Jacobs[9] (Walter Reed Army Hosp) Small inocula of Trichophyton mentagrophyte were placed inside sterilized dialysis bags which were then implanted intraperitoneally into 10 mice At intervals of 1 2 3 4 5 and 12 weeks respectively 1 1 3, 1 2 and 2 of the bags were removed and examined There was no evidence of severe tissue reaction around any of the bags and in none was there any evidence of growth of the fungous inocula Similar control dialysis bags prepared at the start of the experiment and placed in Sabouraud s medium or normal human serum all showed vigorous fungous growth in less than 2 weeks Even after 12 weeks in the peritoneal cavities of mice when the original inocula were removed from the dialysis bags and planted on Sabouraud s medium vigorous growth of the fungus occurred Apparently a humoral factor is involved in the suppression of dermatophytic growth in the living tissues of the mouse which is dialyzable and hence not ordinary protein antibody either natural or acquired

Dialysis bags containing suspensions of T mentagrophytes were placed in 10 small sterile test tubes and 1 cc sterile serum from a healthy donor was added to each tube In 5 tubes the serum was removed daily and replaced with fresh serum from the same donor All tubes were placed on a shaker to keep their contents in circulation After 3 or 4 days fungous growth appeared in all 5 tubes in which the serum was not changed Of the 5 tubes in which the serum was changed daily growth failed to occur in 3 even after 3 weeks whereas in 2 it appeared on the 5th day and was slow and inhibited for another 3 days When the experiment was repeated using serum which had been frozen there was no inhibition of fungous growth even in tubes in which the serum was changed twice daily

(9) J Invest Dermat 31 15 17 Jul 1958

On the basis of these in vitro experiments the demonstration of an antidermatophytic dialyzable substance in human serum is still slightly equivocal and further studies are needed Nevertheless it is felt that there is highly suggestive evidence for the existence of some dialyzable water soluble unstable substance in serum and tissue fluid which suppresses the growth of dermatophytes and permits them to thrive only in those areas of the host not reached by such fluids

► [Interesting findings which help explain why superficial fungi remain superficial Studies such as these should be extended as they could add considerably to our knowledge concerning human susceptibility and defense to disease —Ed]

Esterases in Cutaneous Granulomas G C Wells[1] (Univ of London) examined histochemically specimens of normal and pathologic skin in many dermatoses including chronic granulomas Strong alkaline phosphatase activity was noted in the linings of skin capillaries in the stroma of papillae of growing hairs and in fibrocytes and young connective tissue fibers of scar tissue Acid phosphatase was consistently present in all epithelial structures of the skin with some intensification of concentration at the keratogenous zones In tuberculoid infiltrates acid phosphatase was diffusely present with somewhat greater concentration in giant cell and epithelioid cell masses but was also present in lymphocytic masses and various infiltrates unrelated to infection

With the methods of Holt there appeared to be no simple esterase activity in normal epidermis and its keratin layer except at the mouths of some pilosebaceous follicles and in the intraepidermal portions of some sweat ducts Some acinar cells of sweat glands showed strong esterase activity in contrast to adjacent acinar cells or other sweat glands which might show none Sweat ducts contained a variable amount of simple esterase in their lumens The heaviest concentration of the nonspecific esterase in normal skin was in the pilosebaceous follicle at the point at which the sebum entered the hair shaft canal The sebaceous glands themselves appeared to be esterase negative

The most consistently esterase positive elements of the skin were the scattered dendritic cells of the dermis These histiocytes become more prominent through increase in their esterase content in many chronic inflammatory conditions

(1) Brit J Derma 69 415 4 7 December 1957

of the skin (and other organs?) have the potential for malignant changes and that it is certain growth controlling (inhibitory) factors present in living skin which prevent malignant changes from supervening The latter possibility no longer seems so farfetched in view of the findings of the Sloan Kettering Institute group that patients with malignant tumors have a distinctly decreased resistance to growth and invasion by cultured malignant cells as compared with subjects without malignant tumors—Eds]

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Dialysis bags containing suspensions of T mentagrophytes were placed in 10 small sterile test tubes and 1 5 cc sterile serum from a healthy donor was added to each tube In 5 tubes the serum was removed daily and replaced with fresh serum from the same donor All tubes were placed on a shaker to keep their contents in circulation After 3 or 4 days fungous growth appeared in all 5 tubes in which the serum was not changed Of the 5 tubes in which the serum was changed daily growth failed to occur in 3 even after 3 weeks whereas in 2 it appeared on the 5th day and was slow and inhibited for another 3 days When the experiment was repeated using serum which had been frozen there was no inhibition of fungous growth even in tubes in which the serum was changed twice daily

(9) J Invest Dermat 31 15 17 July 1958

Histologically the true keloid is believed to be a benign connective tissue tumor Though it feels hard it is often edematous and contains thin connective tissue fibers and young fibrocytes

Investigations into Cantharidin Blisters Raised on Apparently Normal Skin in Normal and Abnormal Subjects J H Allison and F Ray Bettley[3] (Middlesex Hosp London) found that patients with atopic eczema had larger blisters containing more protein both absolutely and relative to their own plasma than did normal subjects or patients with other types of eczema of comparable severity Patients with seborrheic hypostatic and nummular eczema had blisters of normal size containing more protein relative to their plasma than did normal subjects Patients with urticaria had blisters of normal size absolute protein content and protein content relative to their own plasma

Blister lids removed from patients with atopic eczema 20 hours after application of 0 2% cantharidin showed many acantholytic cells of a type rarely seen in blister lids from noneczematous subjects The blood leukocyte count was higher than normal in patients with widespread atopic eczema Blister fluid white cell counts were below normal in patients with less than 15% of the skin affected by atopic eczema possibly due to excessive volume of blister fluid formation

Blister fluid in cantharidin blisters may originate from the capillaries or from damaged epidermis If blister protein comes mainly from the capillaries cantharidin must produce greater vascular permeability in atopic and eczematous patients than in normals The fact that patients with urticaria showed blisters with normal protein content although vascular permeability is likely to be more easily produced in this group suggests that the increased permeability in eczema and atopy is due to the action of cantharidin on the vessels being modified by an altered epidermis Histologic studies of blister lids indicate some difference in the degree of acantholysis in the eczema and atopic groups as compared to the control group For these reasons the authors conclude that in the atopic and eczema group the epidermis of apparently normal skin is more readily damaged by cantharidin than is the skin of a normal person The fragility is

(3) Brit J Dermat 0 331 339 October 1958

such as lichenification warts hyperplasia and *acne keloid* In chronic cutaneous granulomas macrophages and giant cells were found to be rich in simple esterase whereas epithelioid cells plasma cells and lymphocytes had more Lepra cells were strongly esterase positive

This survey of hydrolyzing enzymes in cutaneous lesions diverts attention from the relation between these enzymes and infecting organisms (except insofar as the lepra cells are rich in nonspecific esterase) Instead attention is focused on the histiocytes or macrophages which are seen to be heavily loaded with simple esterases in various chronic infections and noninfectious granulomas These cells are distinct from epithelioid and other cells of chronic inflammatory infiltrates and when histochemical methods for esterases have been used their morphology is clear It is not known what chemical part these histiocytes play in the metabolism of foreign material or of damaged tissue

Studies on Keloid Tissues were conducted by E r Wormger and J Zimmer (Univ of Strasbourg) The keloid is not a uniform fibrous tissue Various morphologic characteristics indicate a young connective tissue with active fibrocytes which develop well in edematous surroundings The keloid appears to be rich in water which is bound to the ground substance the latter is different from that of the normal cutis Using the McManus stain the keloid shows heavier staining in the areas of edematous connective tissue than the adjacent normal cutis Electron microscopic studies of keloid tissues also revealed an increase of ground substance over that of the cutis

The authors did paper chromatographic studies on keloid and normal skin tissues in an effort to compare in both the amount of alcohol soluble and ether insoluble amino acid containing substances (*amino acids and peptides*) Nonhydrolyzed alcohol extracts were used which fixed all cells and fibers

Certain cysteine acid compounds (cysteine or homocysteine) are present in unbound form in the cutis and in bound form in keloid tissue also the cutis contains more peptides and fewer amino acids than the keloid tissue The peptides of the two tissues seem to be different in quality Moreover keloid tissue is able to retain more fluid than the cutis

(2) Hautarzt 9 341 346 August 1958

minum salts which are used as deodorants were studied 100 500 μg was required to inhibit growth of the micro organisms commonly found in the axillae

► [Based on the premise that bacteria act on axillary secretions to produce body odor this study demonstrates the effectiveness of hexachlorophene as a deodorant. Of the various substances tested, hexachlorophene was particularly effective in inhibiting the growth of bacteria even when used in the most minute concentrations —Ed]

Effect of Water Soluble Constituents of Horny Layer of Skin on Bacteria First Report H Rockl H W Spier and C Pascher (Univ of Munich) investigated the mechanism of bacterial resistance (auto disinfection) of the skin surface First the water soluble constituents of the superficial horny layer were studied using as culture mediums (1) the watery eluate of the scrapings of the superficial horny layers of healthy persons which was used in unheated and heated (inactivated) form and (2) artificial culture mediums which contained in various combinations the chemical components such as the anions cations urea and amino acids found in the watery eluate of the horny layer

The natural eluate was studied at the usual pH of the normal skin surface pH 5 whereas the artificial mediums were kept at pH 5 7 and 8 The following bacteria were tested on the mediums described Staphylococcus aureus (coagulase-positive) Staph albus enterococcus Escherichia coli and Pseudomonas pyocyanea The natural eluate proved bactericidal for all bacteria This was probably due to a so called high concentration effect and not to the presence of certain antibiotic substance

Of the artificial mediums the addition of α pyrrolidone carbonic acid to the mixture of anions cations NH_3 and urea proved relatively strongly bactericidal for the three types of cocci The mixture of amino acids only proved relatively bactericidal for the two types of staphylococci and for E coli The artificial mediums showed less bactericidal effect than the natural eluate This may be due either to the possibility that the natural eluate contains substances not yet defined chemically or to the method of preparing the artificial mediums since the heated natural eluate showed more similarities in its bactericidal effect to the basically heat resistant artificial mediums

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much greater in patients with atopic eczema than in those with seborrheic nummular or hypostatic eczema

► [The question is whether the normal appearing skin of patients with atopic dermatitis is really normal Our clinical experience leads us to doubt this except perhaps in the very mildest cases Is vascular permeability really more likely to be produced in patients with urticaria than in patients with other dermatoses?—Eds]

Water Content of Stratum Corneum IV Importance of Water in Promoting Bacterial Multiplication of Cornified Epithelium Irvin H Blank and Ruth K Dawes[4] (Harvard Med School) describe a method which permits determination of the moisture content threshold below which a sheet of cornified epithelium will not support growth and multiplication of micro organisms Four representative organisms were studied Micrococcus pyogenes var aureus a nonpigmented micrococcus of the type often found on the cutaneous surface a coliform bacillus and a diphtheroid The moisture requirement for the two micrococci was the same a moisture content of 23 mg /100 mg prevented growth whereas 29 mg /100 mg allowed growth Growth of the coliform bacillus was prevented when the cornified epithelium (callus) contained only 36 mg /100 mg but was permitted by a moisture content of 50 mg /100 mg Diphtheroids failed to grow when the moisture content was 50 mg / 100 mg but grew readily when the content was 70 mg /100 mg These findings indicate that dehydration of the skin resulting from lower relative humidity of the environment might be expected to cause earlier disappearance from the skin surface of diphtheroids and coliform bacilli than of cocci Apparently the range of optimal moisture content of the cornified epithelium is narrow If there is too much moisture the bacterial population increases if too little the skin feels dry

Using hydrated callus as a culture medium the author determined the amount per unit area of various topical antiseptics required to inhibit growth of M pyogenes var aureus Less than 0 1 µg neomycin sulfate/sq cm callus prevented growth of this organism but more than 5 µg bacitracin was required Growth of the micrococcus on hydrated callus was inhibited by 1 µg hexachlorophene or 100 µg benzalkonium chloride No inhibition of growth was observed from 10 µg boric acid but 100 µg caused some inhibition Various alu

(4) J Invest Dermat 33 341 145 September 1959

ba es indicating that the anesthetic penetrates via the fol licle The author believes that the drug passes laterally through the follicular wall at a level near or just below the lower level of the external barrier and goes through the stratum mucosum to reach the papillary portion of the der mis Edema at this point would account for the perifollicular whealing

► [It would be of both theoretical and practical importance to know more about the depth and degre of anesthesia resulting from these topical appl cations Is ane thesia to needle pricks suff cient to allow for scalpel or punch biopsy of an area or for electrodesiccation and curettage of a locali ed lesion? If so this method of anesthe ia might be ideal for the management of selected lesions in children and perhaps even in some adults On the other hand it would be interesting to know if such external expo ure to the local anesthetics tends to result in a higher incidence of allergic s nsiti ation than intracutaneous injection —Ed]

Location of Superficial Epithelial Barrier to Skin Pene tration Samuel Monash (Univ of Miami) compared the percutaneou penetration of topical anesthetics antihista mines and histamine in intact skin and skin in which se lected levels of epithelium were exposed by stripping off cell of the stratum corneum with cellophane adhesive tape Biop ies cf the exact ites stripped and tested physiologically were performed to determine the amount of stratum corneum that had been removed

A compari on of the time required to produce anesthesia on normal skin and on skin stripped 15 times (*thus removing* abc ut half to two thirds of the stratum corneum) showed a diminution with 2% Dorsacaine* 2% Xylocaine* and 2% Pontocaine* ba e olutions of 70 55 and 45 minutes re pectively With 5 more strippings the further diminution in time was negligible The outer 15 strippings therefore form he principal barrier to penetration of the 2% base solutions Similarly with the hydrochloride solutions of these anes the ic drug stripping the skin 15 times resulted in removal of he main barrier to penetration The rest of the stratum c rneum offered little resi tance to passage of the solutions

Hi tamine pho phate in concentrations equivalent to 1 000 of the base when applied to intact skin failed to pro luce a detectable effect On the forearm 10 strippings failed to remove the barrier but after 15 strippings histamine pro luced recognizable changes

The author conclude that the superficial barrier to per

( ) J I est Derm [illegible] 29 367 [illegible] Nov [illegible] 1957

Topical Anesthesia of Unbroken Skin was produced by Samuel Monash[6] (Univ of Miami) in 45 minutes to 1 hour by application of 2% anesthetic base solutions in an alcoholic solvent under an occlusive dressing Drugs used were lidocaine (Xylocaine®), tetracaine (Pontocaine®) phenacaine (Holocaine), procaine benoxinate (Dorsacaine®) and tripelennamine (Pyribenzamine®) The solvent contained 45% isopropyl alcohol, 10% glycerin and 45% water Procaine base required a much longer time to produce anesthesia Similar anesthesia was produced in 1½ hours with 5% anesthetic bases in hydrophilic ointment or petrolatum Both alcoholic solution and ointments produced anesthesia lasting an average of 2-4 hours

Partial anesthesia after 4 hours was produced with 5% anesthetic salts (lidocaine phenacaine and tripelennamine hydrochlorides), respectively in hydrophilic ointment or petrolatum No anesthesia was obtained after 5 hours with procaine hydrochloride With 2% anesthetic salts in aqueous solution anesthesia was produced by the well method (wall of petrolatum surrounding a pool of anesthetic solution) of continuous contact in 2 2¼ hours Anesthesia of the palmar surface was produced with 25% benoxinate base in an alcoholic solvent after a 4 hour application

Pretreatment with ethyl chloride spray for 15 seconds followed by an occlusive dressing of 2% lidocaine base in alcoholic solvent produced anesthesia in 30 minutes on the forearm compared with the usual 45 60 minutes required without such preliminary treatment The addition of 1% sodium hydroxide to 2% benoxinate base in alcoholic solvent resulted in anesthesia in 20 minutes The application was removed after 10 minutes to prevent injury to the skin by the sodium hydroxide

A certain *concentration of anesthetic substance in the skin* is required to produce anesthesia A concentration sufficient to induce anesthesia would seem to be better obtained with anesthetic bases than with solutions of salts because of the greater rapidity with which the more soluble salts are removed by the circulation It has been shown that free bases are lipid soluble penetrating the skin at a greater speed than salts

Perifollicular whealing is observed with some anesthetic

(6) A M A Arch Dermat 76 752 756 December 1957

Studies of embryonal hemopoietic function in subcutaneous fatty tissue has not definitely confirmed Chevremont s conclusions that the fatty tissue represents a latent stage of hemopoietic tissue Blastic nuclei were found in the hypodermis of embryo These coexisted with hemopoietic foci in the dermis structure of fatty tissue was completely preserved and the hypodermic hemopoietic foci were usually pericapillary and probably related to the polyblasts of the capillary perithelium

Existence of hemopoiesis in the dermis mesenchyma observed in all areas examined justifies the conclusion that in other organs besides the skin the mesenchyma possesses the capacity of creating blood differentiations during certain stages of embryonal development and the possibility that this capacity may be revived in pathologic conditions later in life Other investigators have already shown hemopoietic function in pulmonary tissue of the human embryo Pathogenic mechanisms and etiologic factors which may determine pathologic revival of latent dermal hemopoietic function raise clinical and physiopathologic problems of great importance

► [If there is a latent hemopoietic dermal function which could be revived under certain conditions this would indeed be of the greatest clinical and physiopathologic importance Apparently 1 of every 200 cells in the epidermis is a small round cell (Andreasen E Acta dermat. venereol [supp 79] 3? 17 1952) The assumption has been that these small round cells are lymphocytes derived from the blood stream Although this is supported by the beautiful studies of Hagerman (Acta dermat venereol 34 51 1954) there is no proof that all or even most lymphocytes seen in the skin actually are derived from the circulating blood The eosinophil is another cell which perhaps can be formed locally in the skin.—Eds]

Experimental Studies on Behavior of Hyperplastic Rat Epidermis were conducted by Gerd Klaus Steigleder and Waldemar Buchwald (Univ of Frankfort) The way hyperplasia of the rat epidermis develops depends on whether ointment have been applied once or several times The reaction of the epidermis to white petrolatum is not specific but also applies to other ointment bases and probably to rubbing alone There are only quantitative differences in epidermal response Epidermal hyperplasia could be prevented by chloroquine

The authors investigated the effect of white petrolatum on the rat epidermis which had been made hyperplastic by tes

(2) H ta rt 8 505 509 Novembe 1957

embryos and fetuses from 2 months after conception to term showing participation of the skin in hemopoietic function during successive stages of development of the hemopoietic system All regions of the skin were investigated

Dermal hemopoiesis is observed in all cutaneous zones without exception Embryonal dermis consists of completely undifferentiated mesenchyma until the 2d month of intra uterine life differentiation appears in embryos 8 cm long and continues as they grow The first hemopoietic foci are represented almost exclusively by erythroblasts Initial megaloblastic and megalocytic forms are very definite These are replaced rapidly by typical proerythroblasts and erythroblasts Other differentiations of blood appear later beginning at the 5th month of pregnancy and are manifested by mixed hemopoietic sites composed of differentiated blastic cells and mature blood cells Blastic cells of the red series and erythrocytes disappear from the skin in embryo 44 [illegible] cm long i e during the last 2 months of intrauterine life This is probably due to phagocytosis of these element by cells of the white series which appear and develop during these last 2 months

Transformation of mesenchymatous cells in hemopoietic nuclei is manifested clearly in all sections except those taken from fetuses during the last 2 months of gestation The transformation is evident in the form of isolated cells and those not yet differentiated which change into hemocytoblastic elements At this stage it is difficult especially during the last 2 months of the intrauterine period to follow the origin of blood cells since the general hemopoietic system is already advanced at this stage Perivascular and perifollicular localization of hemopoietic foci persists in many cases during the last months This indicates an unquestionable correlation with the polyblasts of Maximov and Danchakova which Marchand identifies with undifferentiated perithelial mesenchymatous cells of perivascular and perifollicular localization of the hemopoietic foci

The lymphoblastic and lymphocytic diffuse and mixed masses found during the last 2 months of gestation and more compact masses in the inguinal region suggest the postembryonal genesis of follicular formations in lymphopoietic organs i e their appearance after cutaneous hemopoietic function

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their effect was examined after an exposure of 22 24 hours Of the fatty acid a well as of the alkyl sulfate compounds those with 12 carbon atoms led most often to erythematous and vesicular skin reactions These compounds were followed in their irritating effect by tho e containing 14 and 10 carbon atoms respectively In the same concentration the alkyl ulfates were more irritating than the sodium soaps

It is suggested that the irritating effect is due to direct cellular damage by the anions freed through hydrolysis

Studies on Cholesterol and Cholesterol Esters in Skin Surface Fats Dorothy B Windhorst and Roscoe C Foster Jr[4] (Univ of Chicago) de cribe a method by which free and esterified sterol fractions of surface fats were separated by column chromatography and the sterol content in both portions estimated by the Liebermann Burchard color reaction The method was applied to scalp and glabrous skin lipids obtained from normal adults

In the scalp surface fats and total and free sterols had the lowest concentration in balding men and the highest concentration in women with nonbalding men occupying an intermediate position No such trend was pre ent in fat from glabrous skin The esterified portion of the sterols represented a fairly constant part of the total fat in all samples both from the scalp and glabrous skin

The lipid film of the skin urface derives from the keratinizing epidermis and sebaceous glands Most cholesterol stems from the keratinizing epidermis Thus the concentration of cholesterol in an ether extract of the skin surface expresses the relative rate of production of both sebum and keratinized cells That balding men have less total sterols in scalp fat as compared to nonbalding men and to women may mean simply that they have an increase in sebaceous gland secretions which i poor in cholesterol or conversely they may have a relative decrease in epidermal contribution The latter possibility a relative decrease in keratinization i attractive since balding scalps universally show a decrease in one form of keratinization—hair formation

Since the esterified portion of the total sterols is present in relatively constant amounts in the scalp surface fat of all persons and in lipid from nonhairy skin the esterification mechanism of sterols in skin surface lipids is apparently con

(4) J In t D mat 29 339 346 N ember 1957

tosterone propionate under various test conditions Also studied was whether the hair cycle could be started with use of testosterone propionate The steroid given daily intramuscularly, in doses of 80 mg/kg body weight led to distinct hyperplasia of the epidermis which set in early and lasted up to 27 days There was no relation between the hyperplasia of the epidermis and the hair cycle The hair cycle could not be started by a 7 or 14 day treatment with testosterone propionate

White petrolatum applied at different times and with varying frequency to the rat epidermis after it was made hyperplastic by testosterone propionate caused no essential changes When colchicine was applied the epidermis made hyperplastic by testosterone propionate showed great increase in mitoses (Dustin reaction) In a control test Chinon ethylen imin (Bayer) a cytostatic agent suppressed hyperplasia of the epidermis after testosterone propionate or petrolatum

Studies on Irritating Effect of Fatty Acids and Alkyl Sulfates of Certain Chain Length on Human Skin were conducted by K H Schulz and G Rose[3] (Univ of Hamburg Eppendorf) Every washing procedure disturbs the physiologic structure of the surface and the superficial layers of the skin The effect of soaps and detergents depends on their composition length of action concentration and pH values and consists of fat removal roughening shifting the pH concentration of the skin surface and of epidermal swelling These changes are reversible within a few hours However persistent clinical changes leading to so called detergent eczema may also develop especially after prolonged exposure

The irritating effect of detergents is certainly not due to their alkalinity only but depends also on their fatty acid and alkyl sulfate content Experience has shown that fats and soaps with a relatively heavy content of fatty acids with a chain length of 10 14 carbon atoms are not so well tolerated by the skin as those containing fatty acids with 16 18 carbon atoms

Sodium salts of saturated fatty acids and alkyl sulfates with an even number of carbon atoms of C_8 C_{18} were tested in watery solution of 0 1 and 0 25% The solutions were applied in small plastic caps directly to the skin and

(3) Arch klin u exper Dermat 205 254 260 1957

sufficient radiation could penetrate through the stratum corneum into the lower layers of the epidermis to effect conversion of provitamin. The vitamin so formed *could then be* readily absorbed into the blood stream. Though the presence of provitamin D in the skin is thought to be related only to formation of vitamin D, it is possible that 7 dehydrocholesterol may play a further role in skin metabolism, possibly in the process of keratinization.

► [At a recent meeting Wheatley exhibited evidence showing that the skin of patients with psoriasis contains a sterol which thus far has not been found in normal skin.—Ed.]

Determination of Layer Thickness of Commonly Used External Medications to Skin was undertaken by H. Ippen and H. Betzler (Med. Academy of Dusseldorf). The thickness of ointment layers may be important in studying resorptive condition or calculating possible toxic effects from drugs applied to the skin. The effective concentration of disinfectant, *antimycotic or anesthetic applications depends on* the amount delivered to the skin. The layer thickness and its possible variations have their greatest importance in the field of skin protective preparations and especially in relation to light protective agents. Their ability to absorb visible radiation is closely related to the thickness in which they are applied and size of the area covered.

The thickness of commonly used ointment bases was determined after their application to various areas of the skin. Hairy areas were avoided. The thickness was calculated from the amount of radiation derived from a radioactive I^{131} containing compound which was added to the base material. The thickness did not depend on the skin area but rather *on the method of* application and type of base material. The mean values of thickness for different materials in microns were: petrolatum 4-10, glycerin cream 9-15, eucerin with water 2-6, paraffin oil 3-6, and a 10% solution of isopropylmyristin in isopropylalcohol 0.25-1.5.

The average thickness of several base materials when applied to the skin varied between 5 and 10 μ. However, the minimal values found are often substantially below the median values. This means that the concentration of active ingredients in skin protective ointments should be sufficiently high to assure protection even when applied sparingly.

► [The layer thickness of the vehicle and concentration of the active

(6) Arch. kl... pe... D rm t. 205: 321-330, 1957.

trolled by a system which operates independently of local factors particularly of male pattern balding Except for the esterified portion the sterols derived from glabrous skin do not follow the pattern of those of the scalp The differences in the free and total sterols in scalp fat observed between balding and nonbalding persons must therefore be a true reflection of local change

Age is an important factor The oldest subjects in any subgroup had the lowest total and free sterol values in fat from the scalp If this trend is primarily evidence for aging rather than for balding then younger balding males show a sign of premature aging in this respect

Presence of Vitamin D Precursors in Human Epidermis Victor R Wheatley and Richard P Reinertson (Univ of Chicago) with the technical assistance of David Sher examined separated epidermis dermis and subcutaneous fat for total lipids 7 dehydrocholesterol (provitamin D_3) cholesterol and cholesterol esters Dried samples of epidermis contained 8 4 16% lipid Epidermal lipids contained on the average 12 times as much provitamin as did the dermal lipid In epidermal lipids 7 dehydrocholesterol accounted for an average of 3 7% of the total sterols compared to 1 6% for dermal lipids Subcutaneous fat contained an average of 0 23% total sterols of which an average of 1 9% appeared to be 7 dehydrocholesterol

The findings indicate that human epidermis contains appreciable amounts of provitamin D The amount present is so high that if it were quantitatively converted to the vitamin about 3 sq in epidermis would give the human daily requirement of the vitamin (400 I U) The exact location of the provitamin in the epidermis is uncertain but it is no longer necessary to postulate that the conversion of the provitamin takes place on the skin surface Others have shown that though radiation of 280 mμ is most effective in curing rickets in rats that of 297 mμ is 80% as effective Sunlight after atmospheric filtration contains little radiation at 280 mμ the usual limit being taken as 290 mμ It has been calculated that at 297 mμ 1/56 of the incident radiation will penetrate 0 1 mm epidermis and 1/3 000 penetrates 0 2 mm The thickness of the stratum corneum has been calculated as 0 04 0 05 mm and of the whole epidermis as 0 07 0 17 mm Thus

(5) J Invest Dermat. 31 51 54 July 1958

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ingredient obviously are of decisive importance in the case of protective ointments creams and lotions As far as topical treatment of skin lesions is concerned however the layer thickness seems to have relatively little importance beyond a certain point except as it may shield and protect the treated area against extraneous effects such as friction changes in temperature air currents etc —Eds]

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